

ISB NEWS REPORT

COVERING AGRICULTURAL AND ENVIRONMENTAL BIOTECHNOLOGY DEVELOPMENTS

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TECHNOLOGY NEWS

BIOINDICATION WITH TRANSGENIC PLANTS

Prior to 1998, transgenic plants were primarily generated to increase the quantity and improve the quality of food, and for cleaning the environment in a process known as phytoremediation. However during that time, scientists from Ukraine and Switzerland also used transgenic plants as biomonitors to assess the quality of environmental surroundings.

Among the first laboratory tests used for biomonitoring were the Ames test and a variety of gain and loss of function tests using *E. coli*-based systems. However, these methods are insufficient for environmental studies of higher eukaryotes. Other previously available analytical methods and laboratory tests were not designed to mimic environmental conditions for the level of pollutant exposure and type of biological interactions occurring in the field. Therefore, alternative methods of field biomonitoring were developed that allowed tests using organisms involved in absorbing and integrating doses of toxicants from polluted water and soils. Animals are difficult to use as model systems in environmental studies, especially in the analysis of chronic exposure effects, because of their unsettled lifestyle. Two major exceptions are zebrafish and land snails. The transgenic zebrafish assay, which uses a non-active *lacI* transgene as a target gene, could potentially be applied to evaluate water quality.¹ Land snails can also be considered as an attractive system for soil toxicity assessment. They live on limited territories and therefore are constantly exposed to local contaminants. However, toxic concentrations of heavy metals need to be relatively high in order to be sensed by these animals.

Classical plant biosensors

Several studies have reported on plants used as biosensors of genetic toxicity in environmental pollutants. Most of the systems commonly used to study mutations in plants were based on the detection of chromosomal aberrations in *Allium cepa*, *Tradescantia*, or *Vicia faba* plants. Among the plant systems that are applied to environmental studies, specific mention should be made of tobacco plants heterozygous for the *Sulfur (Su)* nuclear gene that affects the chlorophyll content of leaves. These plants have been used to study the mutagenicity of different chemicals and could also be used for environmental mutagenesis studies, although the type of the alterations that produce the phenotype is still unknown at the molecular level.

Biomonitoring of radioactive pollution with classical tests

One of the first attempts to monitor the environmental effects of chronic radiation

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was carried out in Japan using the stamen-hair mutation assay, TrSHM, of *Tradescantia*; increased mutation frequencies were correlated with wind direction and nuclear power plant operation periods.² The *Allium cepa* chromosome aberration test was also used for estimating mutagenicity of ionizing radiation. The inhibition of root development in onion bulbs and the increased incidences of chromosomal aberrations in root cells after exposure to radiation were documented.

Recently, we have developed a new microsatellite-based assay for monitoring radiation-induced germline mutation in plants. Thirteen microsatellite loci of two initially genetically-identical populations of wheat (*Triticum aestivum*, L.) grown in either heavily contaminated or clean control soil have been profiled. A marked 6.5-fold increase in germline mutation rate in the parental generation was found among the offspring of exposed plants.³ Of special practical importance is the fact that we could show a statistically significant difference in the germline mutation rate with a relatively small sample size. It should be pointed out that detection of the same increase in mutation rate by standard genetic techniques would only have been possible by using nearly a million plants.

Transgenic plants as pollution biosensors

The systems described above are sensitive and useful, though the changes they (except the microsatellite assay) measure have not been explained at the molecular level. We have now developed new transgenic test plants that provide rapid, cheap, and precise assays of the genotoxicity of radioactively or chemically polluted soils. Both assays are based on the restoration of transgene activity in *Arabidopsis thaliana* plants transformed by a non-active β -glucuronidase (*uidA*) marker gene.

"Plant recombination" assay To develop the "plant recombination" system, *Arabidopsis thaliana* plants were transformed with two overlapping non-functional truncated versions of a chimeric β -glucuronidase marker gene as a recombination substrate. In cells in which the homologous recombination (HR) events occurred at this transgenic locus, *uidA* gene function was restored. Its activity could be precisely located as blue sectors in white plants (see **Figure**). The presence of recombination events represent a measure of the level of DNA strand breaks in the analyzed gene and, by inference, of the plant genome.

We have conducted a number of field and laboratory environmental monitoring experiments using this transgenic *Arabidopsis*. Plants were grown in seven experimental soil plots in the Chernobyl exclusion zone (zone 1), as well as in different areas of the three other contaminated zones (zones 2 – 4). A dose-dependent increase in HR events to 8.4-fold over the control level was detected in plant populations at pollution levels up to 300 Ci/km² in the open field and up to 11.0-fold at pollution levels up to 1000 Ci/km² in the laboratory experiment.⁴

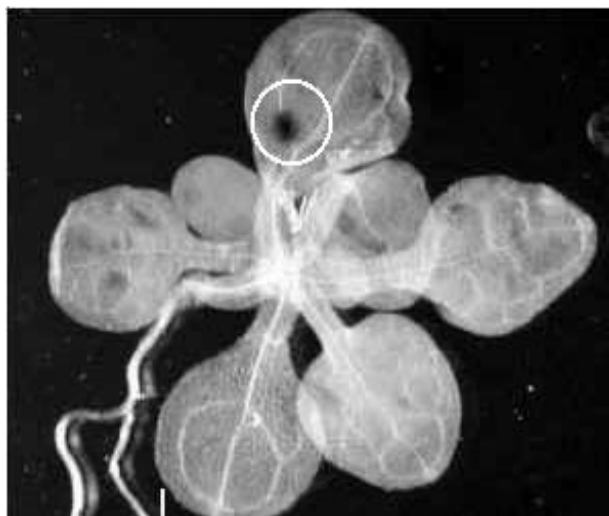


Figure. Recombination and mutation events visualized as blue sectors in an *A. thaliana* plant

“Plant mutation” assay The level of precise repair of DNA breaks is measured by homologous recombination events in plants. However, HR does not show the frequency with which repair mistakes lead to mutations. Somatic mutation events are of a particular importance in plants, since they can potentially be passed on to subsequent generations.

A new method of measuring somatic mutation events in plants has been developed. A termination codon introduced into the β -glucuronidase (*uidA*) gene completely prevented the translation of active protein; transgenic *Arabidopsis* plants carrying these inactivated *uidA* genes were generated. We could observe the spontaneous restoration of *uidA* activity (as blue spots on plants) due to the reversion of the stop codons to the original codons.

Both types of the transgenic systems (“recombination” and “mutation”) were applied to study the genotoxicity of heavy metal ions. Plants sown on media contaminated by the salts of heavy metals, Cd, Pb, Ni, Zn, Cu, and As_2O_3 , exhibited a pronounced uptake-dependent increase in the frequencies of both somatic intrachromosomal homologous recombination and point mutation events. Test plants were also sown in soils collected from sites exhibiting different levels of contamination with Pb, Cd, Zn, and other elements. A four- to sevenfold increase in the frequency of HR and a five- to tenfold induction of point mutations in plants grown in contaminated soils compared to those grown in clean control soil were noted.⁵

The transgenic recombination lines have also been used to evaluate potentially mutagenic exposure to various levels of UV-B radiation. Experiments using specialized sun-simula-

tors revealed that elevated UV-B increases the frequency of somatic HR in a dose dependent manner.⁶ In addition, the system permitted measurement of germline recombination either as a result of an inherited late somatic event or as a meiotic recombination event. Elevated levels of UV-B increased the appearance of plants totally stained blue—that is, plants in which the restoration of the marker gene was inherited by a factor of between two and five.

Outlook

Though several biological systems for evaluating the influence of environmental pollution have been developed, there is no easy test system based on a higher eukaryotic organism yet available. We have introduced a new transgenic plant approach that is fast, sensitive, and in which mutagen-induced HR and point mutation events can be visualized. Since this system allows rapid data collection (around four weeks) and does not require sophisticated equipment and specific knowledge for the detection and scoring of recombination events, it can be broadly used for environmental studies. Soil and water contaminated with metals and organic toxicants pose a major environmental and human health problem that is still in need of an effective and affordable technological solution. We have generated transgenic plants that are able to “sense” the presence of inorganic and, possibly, organic pollutants.

Moreover, these transgenic plants are likely to be useful as phytoremediation devices for removing pollutants from soil and water, accumulating them in their biomass, and detoxifying or vaporizing them. Our plants potentially can be used in remediation quality control tests to evaluate the mutagenicity of contaminated soils before and after remediation. Thus, transgenic plants are beginning to have value as biosensors as well as for the efficient cleanup and post-remediation control of contaminated soil and water. In order to be an effective “alarm system,” the test organism needs to provide a warning of a possible hazard before ecologically significant damage can occur. Plants at the base of the food chain are sensitive to toxicants sooner than those at higher trophic levels, thereby reducing the lag period between exposure and significant impact.

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PLANT RESEARCH

PLANTS FIGHT DISEASE IN THE NEW MILLENNIUM

Based on the major scientific achievements in immunology throughout the past century, it would be reasonable to assume that with the beginning of the new millennium *Mycobacterium tuberculosis*, *Vibrio cholerae*, Hepatitis C virus, rotavirus, and enterotoxigenic *E. coli* would have ceased to pose a significant disease threat to the United States and other industrialized countries. In fact, because countries have become more intricately connected through increased international travel, a greater dependence on a global food economy, and increased immigration and commerce, these well known pathogens have reemerged in mutated and even more virulent forms.

In addition to the reappearance of deadlier strains of commonly known pathogens, the emergence of twenty-nine new diseases (mostly incurable) in the past twenty-eight years underscores our complacency,¹ and, exacerbated by predictions of a burgeoning world population, compels the scientific community to address the question of improved prevention. How can populations be immunized against infectious diseases with improved efficiency and economy?

Diseases of the digestive tract are ranked second only to lower respiratory infections as a cause of death worldwide.² For effective immunization against these infectious diseases in industrialized and developing countries, vaccines must be stable in the absence of refrigeration, easily distributed, and require few or no trained personnel or needles and syringes for administration. Plant-produced vaccines meet all these requirements and have recently been proved effective in immunizing mammals against

rotavirus, enterotoxin, and cholera toxin.³ Several laboratories have demonstrated that bacterial and viral antigens can be expressed in a variety of plant species at levels sufficient to generate protective systemic and mucosal immune responses, indicating that transgenic plants have great potential for the development of oral vaccines.⁴⁻⁵

Mucosal immune responses in the gastrointestinal, respiratory, and urogenital tracts form the first line of defense against invasion by the majority of infectious diseases. While traditional parenteral immunization methods generate a humoral immune response, they fail to induce significant levels of mucosal immunity, permitting bacteria and viruses the opportunity to proliferate in the body's tissues prior to contact with the cells of the immune system. Therefore, infected individuals can display symptoms of illness before the body's immunity mechanisms begin to fight off the invaders. Mucosal immunization generates secretory antibodies, which intercept the pathogen at the mucosal surface, preventing the initiation of infection. Plant-based vaccines can maintain the integrity of antigens even in the acidic environment of the stomach. Due to the rigidity of plant cell walls, which resist immediate digestion by stomach acids, pancreatic proteases, and other degradative enzymes, antigens are slowly freed from plant tissues when digested and released relatively intact into the small intestine.

In addition to the obvious utility of producing a low cost vaccine protein, transgenic plants offer a variety of additional advantages, some of which are unavailable through parenteral immunization. These advantages include the ability of plants to express large complex antigens without compromising immunogenicity, the absence of animal pathogenic proteins, and the avoidance of equipment-related safety issues. The first reported vaccine candidate to be expressed in transgenic plants was the cell surface-adhesion protein Spa A, or streptococcal antigen I/II, from *Streptococcus mutans*, the major bacterial cause of tooth decay.⁶ The *spa A* gene was introduced into tobacco by *Agrobacterium*-mediated transformation, and the protein expressed at levels of up to 0.02% total leaf protein. This study is significant because Spa A is a large protein, over 1,500 amino acids, indicating that plants can accommodate insertion of genes expressing proteins of considerable size.

Three major enteric diseases resulting in debilitating and deadly diarrhea, which kills millions of people annually, are cholera, rotavirus, and enterotoxigenic *E. coli*. Genes encoding antigenic proteins from all three pathogens were incorporated into a plant-synthesized multi-component vaccine. In early immunization experiments, McKenzie and Halsey confirmed that when the cholera toxin B (CTB) subunit was covalently conjugated to an antigen, mucosal



antibodies were formed against the antigen proteins.⁷ The CTB subunit was fused with rotavirus and enterotoxigenic *E. coli* antigens and expressed in transgenic potato.³ The CTB subunit protein was able to bind to G_{M1} ganglioside receptors located on the mucosal epithelial cell surface. The presence of significant levels of mucosal and systemic antibodies, made in response to oral immunization with the plant-delivered antigens, indicated that CTB was an effective carrier for delivery of the enteric pathogen fusion proteins via food plants.

Traditional methods of vaccination against cholera demonstrated that memory B cell populations decline in three to six months after antigen injection to levels low enough to make individuals susceptible to reinfection. While re-immunization may be practicable for individuals in cities, it is costly and not easily available to people living in rural areas. Low compliance to immunization schedules perpetuates reinfection by the endogenous pathogens. Plant-based vaccines are a more feasible source of immunization, because farmers in rural areas could potentially grow vaccine-containing plants indigenous to their own regions, making use of local agricultural techniques and available agricultural machinery for cultivation and harvest.

The biological activity and immunogenicity retained by pathogen proteins produced by transgenic plants is due in large part to the presence of plant chaperone proteins, homologous to mammalian chaperonins, which insure correct folding of the foreign proteins once they exit the endoplasmic reticulum. Chaperone proteins maintain order in the crowded cell cytoplasm. They function to prevent newly synthesized cytoplasmic protein chains from associating with incorrect protein partners by mediating the folding of proteins into their quaternary structure.

Although plant-based vaccines offer a variety of advantages over parenteral immunization, one limitation is the relatively small quantity of recombinant protein that is synthesized in edible plants. Plants do not normally utilize foreign proteins and little energy is spent in their synthesis, resulting in low yields. To circumvent this problem, our laboratory adopted the strategy of using bacterial toxin peptides for targeting antigens to gut cells. This approach increased mucosal and systemic immune responses to the recombinant protein synthesized by the plant. The non-toxic, cholera toxin B-subunit binds to G_{M1} ganglioside on receptors embedded in the enterocyte apical surface, facilitating CTB-antigen fusion protein delivery to the lymphocytes of the gut-associated lymphoid tissue.

The instability of recombinant antigens following exposure to heat produced from conventional cooking methods is

another issue that impacts plant-based vaccine protective efficacy. Thus far, successful attempts to produce vaccines in palatable uncooked plants have been limited to tomatoes and lettuce. It is important to engineer vaccine proteins into a variety of food plants, since one type of plant may only be available seasonally or in a specific geographical location. Further, many plants grow under restrictive climatic conditions, and the availability of a variety of engineered plants will avoid expensive distribution costs.

The last hurdle that plant-based vaccines may face before they are widely accepted is not proving their scientific feasibility but overcoming public apprehensions. The pioneers and champions of plant-based vaccines will need to combat the present ignorance of plant-based vaccines, impeding their acceptance. Research should focus on the safety of plant vaccines, the examination for possible allergenicity or toxicity of individual proteins transferred into food plants, and dose response studies in mammalian systems to indicate the possibility for immunotolerization following prolonged exposure to antigen proteins in the diet. Answers provided by these studies will accelerate the impact of plant-based vaccines for improved health.

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BIDIRECTIONAL EXPRESSION VECTOR FOR PLANTS

Biotechnology researchers have shown much success over the years in engineering transgenic plants to express divergent traits ranging from *Bt* toxin to animal antibodies. Perhaps the greatest accomplishment involves regulation of a single gene to alter the synthesis of proteins or the direction of metabolic pathways. However, alteration of single-gene characteristics is but a small component of future plant biotechnology methodologies. New strategies for providing customized plants will involve the synchronized expression of several genes.

Regulating the simultaneous expression of two or more genes is necessary for the co-production of multiple compounds in a single organism and constructing subunits for multiunit proteins. It is a challenging task to engineer multigene characteristics using traditional single gene expression systems.¹ According to research published by Mingtang Xie, Yuehui He, and Susheng Gan at the University of Kentucky in Lexington, a technique using bidirectional control of promoters may offer a superior means of achieving synchronized multigene expression.²

The authors used traditional polar promoters to direct the bidirectional expression of two genes. The novelty of their technique was in locating the promoter between the two desired genes, in contrast to the traditional approach to tandem gene expression that places a unidirectional promoter upstream of the genes. Gan's team converted the enhanced constitutive CaMV35S promoter to a bidirectional one by attaching a 35S minimal promoter to its 5' end in opposite orientation so it could direct expression of a second gene. A series of vectors were then made:

pGlb1 = *GUS* fused to 35Smini fused to CaMV35S plus a downstream *NPT II*;

pGlb2 = *GUS*, CaMV35S, *NPT II*;

pGlb3 = *GUS*, SAGmini, CaMV35S, *NPT II*;

pGlb4 = *GUS*, 35Smini, PCISV, *NPT II*;

pGlb5 = *GFP*, 35Smini, *OPRI*, *GUS*; and

pGlb6 = *GUS*, 35Smini, *OPRI*, *GFP*.

(PCISV is a peanut chlorotic streak caulimovirus promoter; *OPRI* is an inducible promoter that encodes a reductase which likely promotes jasmonic acid biosynthesis; *NPTII* is the neomycin phosphotransferase gene; *SAG* is a senescence-specific gene in *Arabidopsis*; *GUS* [β -glucuronidase] and *GFP* [green fluorescent protein] are reporter genes.)

The vectors were introduced into *A. thaliana* using an *Agrobacterium* transformation system. The team was able to show *GUS* expression in all antibiotic resistant transgenic

Arabidopsis T₁ lines except pGlb2. As expected, *GUS* expression was minimal in the pGlb2 vector, which shows that the minimal sequence is needed for bidirectionality. Their work thus demonstrated that bidirectional expression is possible in constitutive and nonconstitutive control elements, and the ability of a promoter to be rendered bidirectional is not an inherent characteristic of the particular promoter.

Bidirectional promoters naturally occur in a variety of eukaryotic organisms. Joel Chandless's lab at the University of Rhode Island reported discovering a novel bidirectional promoter in *Arabidopsis thaliana*. The functionality of the promoter was analyzed using a chimeric gene construct containing phosphinothricin resistance (BAR) as a selectable marker and *GUS* as the reporter gene.³ Initial trials confirmed Gan's research by demonstrating the feasibility of using the promoter in plant transformation systems.

Other plants contain bidirectional promoters. Alerone pigmentation in maize is under the control of a bidirectional promoter as shown by researchers in 1998 at the University of Wisconsin, and a bidirectional *ORFII* promoter in *Brassica napus* has been investigated at the John Innes Centre in England.

Promoters with bidirectional activity are reported regularly in animal studies. Avian genes coding for purine nucleotide biosynthesis were co-expressed using a bidirectional promoter identified by Howard Zalkin at Purdue University (Indiana) in 1993. Splitting the promoter induced separate control of upstream and downstream cognate genes. Kenneth H. Gabbay and coworkers of Baylor College of Medicine (Texas) used an aldehyde reductase bidirectional promoter to express firefly (*Photinus pyralis*) and sea pansy (*Renilla reniformis*) reporter genes. The ras2 promoter of fruit flies, the workhorse of animal gene regulation studies, exhibits bidirectional activity, as is true for the related c-Ha-ras1 in humans and c-Ki-ras in mice.

Researchers at the Chinese Academy of Science (Beijing, China) found a bidirectional promoter in the cotton leaf curl virus (CLCuV) isolated from infected tomato leaves. They cloned the gene to *GUS* reporter and nopaline synthase terminator genes and achieved strong expression on both ends of the promoter in tobacco and cotton leaves. The research by Gan et al. and successes of other recent researchers using unidirectional promoters from plant viruses is encouraging for future applications of a CLCuV expression vector. Other research reveals that fungi also contain bidirectional promoters used to control complex biosynthetic pathways.⁴



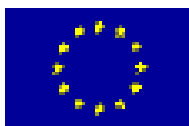
In his paper, Gan argues that expressing multiple genes with the traditional setup using a single upstream promoter can lead to gene silencing through repeated use of the promoter. Gan's prediction of the utility of bidirectional genes for co-expressing multigene traits in GMOs is supported by the work of Chandlee, Gabbay, Liu, Meng, and Zalkin. Gabbay also concluded that, at 200 base pairs, the compact nature of the bidirectional promoter he identified saves space on vectors. Commercial applications using bidirectional promoters are already making their way to market. For example, a synthetic bidirectional vector called the Tet Expression Vector is commercially available through CLONTECH (California) for use in cancer cell lines. Gan's work provides incentives to develop more bidirectional systems for plants.

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REGULATORY NEWS



EUROPEAN COMMISSION'S PROPOSED END TO MORATORIUM AROUSES LIVELY DEBATE

The European Union has not authorized a genetically engineered (GM) product since October 1998. This has caused major trade friction with the US and has created a setback for European agbiotech companies. Last January, the European Commission published a White Paper on

Food Safety, which proposed the establishment of an independent European Food Authority (in place by 2002), and a food policy that included food labeling and the traceability of food and food ingredients. In July, the Commission adopted two proposals that reflect concepts presented in the White Paper and that are designed to end the *de facto* moratorium on GM product approval.

Present Law on GM Food

Current legislation governing GM crops and foods is embodied in a complex mixture of Regulations and Directives. Regulations have a direct force of law on Member States, whereas Directives provide policy objectives, which must be transformed by each Member State into national law. Although Directives offer flexibility on the precise form of national legislation, Member States cannot simply disregard a Directive. This is illustrated by the Commission's recent announcement that it is taking seven Member States to the European Court of Justice for failing to enact enabling legislation to implement an amendment of a Directive (90/219/EEC) on the contained use of genetically modified microorganisms. The European Commission, the executive institution of the European Union, initiates legislation, presents legislative proposals to Parliament and the Council, and implements legislation adopted by Parliament and the Council.

Significant current law includes Directive 90/220/EEC, which created a notification and risk evaluation process for placing a genetically modified organism (GMO) on the market. According to this scheme, once the GMO is authorized, it obtains free circulation in the European Union, although it can be temporarily prohibited if a Member State believes that the GMO poses a possible danger to public health or the environment. Two GM products were approved under this Directive: glyphosate-tolerant soya beans (1996) and GM maize, which expresses *Bacillus thuringiensis* endotoxin and has an increased tolerance to glufosinate (1997).

Regulation (EC) 258/97 provides for the compulsory labeling of novel foods and food ingredients that contain GMOs or that have been produced using genetic techniques. Novel foods or food ingredients derived from GMOs, but not containing GMO material, must only be labeled if they are no longer "equivalent" to conventional foods.

Following the approval of GM maize, Austria, Italy, and Luxembourg introduced national provisions prohibiting the use or sale of GM maize in their countries. In response to these concerns, the Commission adopted Regulation (EC) 1813/97 in September 1997 providing for the compulsory

labeling of GM soya and GM maize, which had been approved before the Novel Foods Regulation came into effect. Labeling regulations were further modified by Regulation (EC) 49/2000, which set a *de minimis* threshold of one percent for GM material present adventitiously in non-GM material, and by Regulation (EC) 50/2000, which requires the labeling of food and food ingredients containing additives that have been genetically modified or have been produced from GMOs.

At this time, labeling requirements are triggered by the presence of GM protein or GM DNA in the final product. Current regulations do not require labeling if the product was derived from a GM source but does not contain the novel protein or DNA.

The Proposals

In its draft regulation on GM food and GM animal feed, the Commission explains that the proposal covers products “produced from a GMO,” but not products “produced with a GMO.” The former term indicates that a portion of the end product, whether it is the food or feed itself or an ingredient of the food or feed, has been derived from GM material. The latter term indicates that the product was made with the “assistance” of a GMO, but that no material derived from the GMO is present in the end product. An example of a “product produced with a GMO” is cheese made using GM enzymes.

The Commission proposes to regulate products made from a GMO by establishing a “one door – one key” procedure under which it would be possible to file a single application for the deliberate release of a GMO into the environment and for the use of the GMO in food or feed. The European Food Authority would perform scientific risk assessments with regard to the environment and human and animal health safety. Based on the opinion of the European Food Authority, the Commission would then draft a proposal for granting or refusing authorization, and the proposal would have to be approved by a qualified majority of the Member States within a Regulatory Committee. The Commission contemplates that the initial authorization would be granted for ten years and renewable for ten-year periods. Recalling the US experience with StarLink, the Commission requires that GMOs that are likely to be used as food and feed can only be authorized for both uses or not at all.

The Commission plans to continue the labeling exemption for the accidental presence of GM-material in food up to one percent. However, the proposed regulation on GM food and GM animal feed would repeal provisions in the Novel Foods Regulation that provided a simplified proce-

cedure for GM foods that are substantially equivalent to existing foods. The reasoning is that, although substantial equivalence is a key factor in the safety assessment process of GM foods, it is not a safety assessment in itself. Thus, in a major break from current practice, the proposals extend labeling requirements to end products, regardless of the detectability of GM DNA or GM protein. As an illustration, the proposed regulation would cover refined maize oil made from GM corn.

Since analytical methods will be insufficient to determine whether refined ingredients have been derived from a GM material, the Commission proposes to control the accuracy of information provided on labels through a traceability system. At present, there are no specific traceability requirements for products that contain GMOs or that are derived from GMOs. The proposed regulation places new obligations on business operators to transmit and retain information at each stage of market placement so that it will be possible to trace GMOs through the production and distribution chain. According to the Commission, this traceability system will reduce the need for sampling and testing of products.

The proposed regulations reflect an effort to balance the concerns of consumers, environmental groups, and industry. Yet the proposals appear to have pleased no one.

Reaction to Proposals: EEYUU, EU

Although environmental groups praised the concept of a tougher labeling system in general, they voiced concern over the specifics. Characterizing the proposal as an inappropriate reaction to threats from the US and GMO-producing companies, Greenpeace took the position that the one percent threshold for accidental trace presence of GM material was too high. Echoing this sentiment, German Environment Minister Renate Kunast attacked the “trace” exemption, insisting that a system of zero tolerance is the safest course.

Friends of the Earth, who referred to the adventitious presence provision as a license to pollute, calculated that the buffer zone between GM crops and non-modified crops should be increased to over three miles to save conventional farms from GM crop “contamination.” Some have speculated that it would not be possible to maintain the required buffer zone without making it impractical to grow GM crops entirely. In contrast to those protesting any standard above zero tolerance, trade and industry sources reportedly stated that five percent is a more feasible limit, and that, if adopted, the new labeling rules could prevent the import of most food into Europe.



US farm groups criticized the proposed traceability scheme, calling it unworkable, and said that the extra burden on producers could damage billions of dollars of exports to the European Union. According to US trade representative Robert Zoellik, the proposed regulations present impractical regulatory barriers that extend far beyond health protections. The United States has proposed a labeling system based upon the testing for GM material in the final product. However, EU Food Safety Commissioner David Byrne has insisted that the proposed labeling strategy guarantees food safety and transparency “from the farm to the fork.”

Another criticism from the US is that the new rules do not apply to major European products made with GM material, such as wine, cheese, and yogurt (i.e., the Commission’s products “produced with a GMO”). This is one illustration, US officials say, of how the proposed regulations would treat US products less favorably than European products. Discrimination is inconsistent with World Trade Organization requirements, and the US Administration is being urged to file a legal case before the WTO as soon as possible.

The proposed regulations are subject to co-decision with the European Parliament and the Council and are expected to enter into force in 2003 at the latest.

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REPORTING IN: THE NEW ZEALAND ROYAL COMMISSION ON GENETIC MODIFICATION

On the 30th of July 2001, the results of the first national open debate on genetic modification (GM) and associated technologies were made public. After fourteen months of consultation with advocates and opponents of GM, the Royal Commission on Genetic Modification (RCGM), an independent review panel, produced a 1200-page report that provided 49 recommendations for changes to government policy, regulatory legislation, public institutions, and the future direction of biotechnology and associated research. Based on a mandate to consult extensively with the community and to identify and assess the strategic options available to government, the result is a document that will inform public debate worldwide. The full text is accessible at: <http://www.gmcommission.govt.nz/index.html>.

The RCGM operated its public consultations in the style of a courtroom rather than a parliamentary debating chamber or a select committee. They received presentations and participated in adversarial cross-examinations of representatives of the public, research institutes, environmental groups, biotechnology companies, and farmers, endeavoring to hear the views of all, not just the most vocal. This level of consultation is unprecedented in the GM debate and was only possible due to several conditions unique to New Zealand. An island country with relatively secure biological border controls, New Zealand has the option to exclude genetic material it deems unwelcome such as that of viruses, weeds, vermin, and, potentially, GM organisms. Furthermore, Maori cultural values (which have also been partially adopted into mainstream culture) stress the common ownership and, to some extent, inviolability of New Zealand’s genetic heritage. The economy is dependent upon the export of agricultural commodities and also on tourism, both industries that rely on the country’s self-branding as ‘clean and green’. Most agree that ‘clean’ is synonymous with unpolluted and, for some, ‘green’ is the antithesis of GM. As in many countries, the fledgling New Zealand biotechnology industry had agreed to a voluntary moratorium on the open release of GM organisms.

As a result of exposure to all sides of the question, members of the RCGM determined that careful use of GM technology in New Zealand is an opportunity foolish to discard. They also advocated the expansion of other agricultural methods, stressing that coexistence of GM organisms with non-GM material is entirely possible and,

for New Zealand, economically desirable. This outcome was to be expected and perceptive commentators had predicted it.¹ Given the range of issues the Commission was required to cover, a compromise result was to be expected, although this has allowed accusations of hedging and ducking of difficult decisions.

The RCGM was required to consider the impact of GM technology on New Zealand via three criteria sets: cultural/ethical/spiritual; environment/health; and economic/strategic. Many groups on both sides of the debate focused on one of these to the exclusion of other issues—such groups will rarely be satisfied with a compromise that takes other issues into account. Many who advocate the use of GM technology were concerned that the Commission would be swayed by emotive arguments, be misled by poor science and factual misrepresentation, and would fail to take the long-term view. Conversely, many who oppose biotechnology were concerned that the Commission would be swayed by economic arguments, be misled by biased science and misrepresentation, and would fail to take the long-term view. Could any report satisfy both sides?

Responses and consequences in New Zealand

The politically strong Green Party of Aotearoa New Zealand was actively involved in setting up the RCGM. They argued that re-branding New Zealand as ‘100% organic’ (where ‘organic’ is defined to exclude GM commodities) would provide an economic advantage. The RCGM agreed that ‘organic’ was an important branding, but saw the greatest advantage in not limiting New Zealand to one fashionable niche market. The Green Party’s response has been muted but largely uncomprehending—their leader said in one interview “we just couldn’t see how they could come to those conclusions on the basis of what they heard.”² Other mainstream political parties have cautiously welcomed the report as a document on which to base future policy decisions but have yet to respond in detail or offer changes to their manifestos. The government will not give its official response to the RCGM before the end of October.

Other politically-minded environmental groups have voiced stronger opinions. Greenpeace criticized the RCGM for inadequately applying the controversial Precautionary Principle.³ As in many of the responses to the report by anti-GM groups and individuals, they stressed that over 90% of the 11,000 public submissions to the Commission were opposed to the open release of GM organisms. The RCGM anticipated this objection and emphasized that “this was an independent inquiry, not a referendum.”⁴ The inaccuracy of statistics derived from volunteer opinion polls

is well known. A further response by these groups has been to organize street-level protests to encourage public participation. There are anecdotal reports of factual misrepresentations of both the report’s content and GMO characteristics at such events.

Researchers and the biotechnology industry have responded positively to the compromises recommended in the report. The fact that only one side was calling for the complete rejection of the other’s point of view was acknowledged by the RCGM: “No submitters suggested [the unrestricted use of genetic modification technology] to us.”⁵ Scientists presenting to the RCGM advocated safe, cautious use of GM technology; they were encouraged when the RCGM recommended that the voluntary moratorium end and pleased that a biotechnology future had not been foreclosed. According to industry representatives, if all the recommendations of the RCGM are adopted into statute, the regulatory machinery protecting workers and the public will be optimal and appropriate to the levels of risk and return.

The industry has since made public statements acknowledging that the RCGM has laid the groundwork for future debate, whereas the anti-GM faction has focused on how the RCGM failed to present a final, satisfactory answer. These interpretations may reflect the relative priorities of the two sides, that is, business economics versus social politics or their intellectual underpinnings. The debate will undoubtedly become more heated when the recommendations regarding labeling of GM products are embodied into law—a topic on which the industry is divided while GM opponents are united. Another disappointment for industry was the RCGM recommendation that New Zealand employ sterility technologies to contain GM; use of these techniques is objectionable to both many scientists and political environmentalists.

The Commission also recommended that only animals that are separated from the human food chain can be used as bioreactors. Though this recommendation could be interpreted to represent the need for appropriate physical containment of such animals, it could also mean that researchers can use as bioreactors only those species never farmed for protein. The latter interpretation might significantly limit the options for the industry and its advantageous access to New Zealand’s substantial agricultural resources and expertise. Also, the industry has yet to comment publicly on the fact that several of the RCGM’s recommendations, taken together, allow the ‘organic’ industry to claim large areas of productive farmland to the exclusion of GM produce, stifling competition and limiting resources.

New Zealand has unique natural resources that could be used to great benefit in both medical and agricultural research. The RCGM expressed its support of cultural and intellectual property rights for indigenous people internationally and recognized the need to protect the traditional knowledge and biota valued by the Maori. This support is likely to be popular in New Zealand, but, in practice, an appropriate framework that adequately addresses Maori concerns may be a long way off. Therefore neither Maori traditional knowledge nor New Zealand's unexplored natural resources are likely to be used to their best advantage in the immediate future.

End of the process, start of the process

The RCGM report has been favorably received by the international scientific community.⁶ The comment has been made that an admirable level of scientific rigor was applied to the vast pile of submissions received by the RCGM, which consisted of a judge, a cleric, a scientist, and a teacher. Their report is an attempt at a balanced, workable compromise that would be applicable in many contexts. As such, it naturally disappointed both sides to some degree but probably offers the best way forward. For New Zealand, the adoption into statute and policy of all the RCGM's recommendations would benefit the industry, the anti-GM lobby and, most importantly, the public. Other countries will observe that, after extensive consultation, the RCGM did not endorse GM technology unreservedly or ban it completely. It advocated sensible modifications to the existing regulations governing GM products to make them reflect the realities of current research, improving safety and yet allowing progress. It recognized the worth of the 'organic' marketing label and implied organic produce's superiority over GM products. It recommended segregation rather than integration. It called for the codification of a long-term national strategy for biotechnology and greater involvement from all interested and affected parties. These changes would likely improve the debate in all countries.

The RCGM process afforded all sides a chance to present their best case, and exposed factual error and unfounded hyperbole when it was encountered. It is important to recognize that the RCGM report suggests that its recommendations are fundamentals and all subsequent debate should revolve around them. The report is a complex document that lays out the arguments cogently and comments on them intelligently and without bias; it is therefore a unique document, which can be used to inform the debate from all sides in the future. The contributors should acknowledge that the report does not provide all the answers—the job is far from complete. The process by which the 49 Recommendations of the Royal Commission on Genetic

Modification are turned into guideline, statute, and policy in New Zealand and elsewhere will be long, and will make these the most interesting of times.

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