The Significance of Transgenic Plants for Developing Countries

Featuring

- Biosafety
- technology transfer
- socio-economic impacts

transgenic papaya

Basel Switzerland

November 29 – Dezember 1, 1999

Organizers

Agencies BATS and BICS of the Swiss Priority Programme Biotechnology, Basel, Switzerland
United Nations Industrial Development Organization (UNIDO), Vienna, Austria

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Biotechnology of Parasitic Weed Control; A Parable of Unmet Needs, Varied Potential Solutions, Impediments and Risk Analyses

The flowering witchweeds (*Striga* spp.) parasitize the roots of all major grain and legume crops in sub-Sahara Africa, to the extent (according to the FAO) of halving yields of 100 million people. The flowering broomrapes (*Orobanche* spp) parasitize the roots of major vegetable and legume crops (as well as sunflowers) throughout the Middle East including chickpeas and broadbeans that are protein staples. There are no broadly usable crop-selective chemical mechanisms to control parasitic weeds underground, and there is a paucity of crop varieties with natural genetic resistance to these parasites. Genetic engineering permits the transfer of genes for either herbicide resistance or parasite resistance from wherever they occur, into chosen crops, after the genes have been pinpointed and isolated. Genetic engineering could also assist in rendering biocontrol agents more virulent, such that they could be readily utilizable.

Despite the vast market potential for any potential solutions, commercial entities view the markets where parasitic weeds are rampant as too poor for development of new products or varieties. Herbicide resistance is a case in point, as the genes, transformation technologies and herbicides are available. The choice of genes for resistance to systemic herbicides is limited to only target site resistances where the herbicide can be translocated to the parasite, inhibiting a metabolic pathway of the parasite. Some target site mutated as well as engineered crops appropriate for parasitic weed control are already marketed in the developed world for other purposes. We have used them to demonstrate that the control of parasitic weeds is excellent, and yet there was no measurable crop damage. Breeding material or gene constructs for such resistances should be contributed by the private sector that owns them to the public sector for the transfer of resistances into varieties used in areas infested with these parasites. Most commercial entities have not been forthcoming. CIMMYT has used marker-assisted breeding to transfer a herbicide-resistant acetolactate synthase gene, not patented in Africa, from American maize into varieties adapted to Kenya. Together we developed seed dressing technologies precluding the need of sprayers, requiring less than a tenth as much herbicide per hectare, and allowing spaced intercropping with legumes, and the material is now at the level of large scale testing in farmers' fields. We have also developed seed dressing techniques with asulam and glyphosate, for use on their respective transgenically-resistant crops, which have been verified in the greenhouse with *Orobanche.* The genes would have to be made available so that this could be tested with *Striga.*

Transposon tagging has allowed CIMMYT to isolate putative maize mutants with a high degree of resistance to *Striga.* This method allows them to physically isolate the gene conferring resistance, and to engineer the mutated form into maize as well as other species. Biocontrol agents have been isolated that could be used to control both parasitic weeds. Some aspects, such as formulation of cheaply produced mycelia, instead of costly spores, have been partially solved. The organisms could still retain their high degree of specificity even if genes conferring hypervirulence were introduced by genetic engineering. Such genes might be the difference between success and failure with such an approach. We have engineered marker genes into two *Orobanche*-attacking *Fusarium* spp. so that we can follow their movement in the soil, in colonizing the crop, and while attacking the parasite.

A new biotechnological approach has been promulgated for controlling *Striga hermonthica* deals with *Striga* itself and not the crop host. It is based on the premise that *Striga hermonthica* is not a wild species, it is a weed and like other weeds, it was co-domesticated with crops, and like crops, cannot exist in the wild as it has few wild hosts especially in East Africa. The strategy proposed is to use genetic engineering to reverse evolution; i.e. to force *Striga* back to being an innocuous wild plant. It is designed to lead to self control of *Striga* using genetic engineering to debilitate *Striga* by TAC-TIC, a system conceived for insect pest control using “Transposons with Armed Cassettes for Targeted Insect Control”. This would entail transforming *Striga* with high copy number transposons carrying assisted-suicide “*kev*” (Kevorkian) genes. *Striga* carrying deleterious transposons (DTs) with *kev* genes will quickly spread the genes throughout field populations because *S. hermonthica* is an obligate outcrosser requiring cross pollination. The *kev* genes can then be activated, and debilitate the parasite. The *kev* genes could be introduced within the Ac transposon, which transposed and proliferated in all plant species tested.

Whereas transgenic maize carrying genes such as glyphosate resistance is readily imported into Africa for consumption, it may not be planted out (though the farmers are not aware of this). The decision making processes are not fully activated for introduction and field experimentation with transgenic crops, not even for crops such as maize that have no wild relatives in Africa, nor for genes already present in the world and African market place. The quarantine authorities do not seem to have yet given considered thought to the regional movement of potential biocontrol agents, not even ones that are non-transgenic, or even ones that are endemic. Biotechnology has much to offer in solving the problems from parasitic weeds. Methods must be set in place for evaluation of the risks and the benefits that the different strategies can provide for different crops and agroecosystems, so that more solutions can rapidly get to, and benefit the farmers and the economies of developing nations.

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Can Technology Assessment ease Technology Transfer?

Distinct characteristics of technology assessment (TA) processes are (1) assessment of the state and impacts of a technology, and on the organizational level (ii) bringing together knowledge from different scientific disciplines (pluridisciplinary approach), decision makers and stakeholders that may be affected by new technological developments.

In order to estimate possible benefits of TA, the basics of technology transfer (TT) need to be remembered. TT is the process of converting natural science knowledge into techniques, i.e. into means to reach certain societal or economic goals such as securing food supply or attaining economic advantages, respectively. Whereas TT has long been a spontaneous process, this has changed with the scientific background of technological development becoming more and more complex. In addition, the scale of technology applications has dramatically increased ecological and social impacts.

In this situation a holistic system's approach to TT has become urgent. Results of TA studies offer astonishingly valuble assistance for a comprehensive management of TT. Areas which benefit from TA are (i) science policy formulation and R & D project management, (ii) technolgy shaping, (iii) development of monitoring programs for large scale applications, and (iv) societal anchoring of technology.

Science policy formulation and R & D project management

The challenges in arriving at policy options for high technology are rapid change, complexity, interdependency, environmental and societal implications. Due to financial and capacity limitations, maintaining focus on priority issues is crucial. Since research programmes are longterm endeavours, a careful but efficient interdisciplinary approach is essential. As it has been mentioned, a TA process can offer a most holistic result with respect to the organization and control of research and development projects.

Technology shaping

Although it may be still early to conclude on the influence of TA on the development of genetic engineering, it is clear that the ongoing debate on this technology has already exercised a profound influence in several ways: (i) improvement of knowledge base for decision making, and (ii) prevention of the undesirable, promotion of the desirable in technology developments. Examples for the influence of the genetic engineering debate on technology shaping are (i) the use of antibiotic marker genes, (ii) the investigation of plastid transformation as an alternative for nuclear transformation, and (iii) the abandonment of terminator technology.

In order to shape modern biotechnology for a useful contribution to technological development it is important that detailed criteria and indicators are defined on social preferences. If, for example, the concept of sustainable development is adopted as a guideline for evaluating our technological activities, then one would need to provide a general criteria catalogue for the ecological, economic and social dimensions. This could be a constructive outcome of the technology assessment, which will continue to be a valuable tool in accommodating the pluralistic nature of individual value systems in society.

Development of monitoring programs for large scale applications

When ecological impacts of open biotechnological applications (deliberate releases) are assessed, there remains an inevitable degree of uncertainty, since safety is never abolute. Safety is defined via tolerable damage or risk thresholds. TA will reveal which of the possible hazards may require monitoring in order to verify assumptions made during safety assessment. In this way, case specific monitoring programs can be elaborated.

Societal anchoring of technology

Again conclusive analysis of the influence of TA may not be possible yet. However, the practice of TA has clearly resulted in the following positive outcomes:

- Increased understanding of issues (e.g. safety is not longer viewed as a one facet topic).
- Rationalised debate due to better understanding of genetic engineering.

- The ability to differentiate amongst the various gene technology applications (e.g. higher acceptance for medical applications).
- Clarified argumentation basis; certain arguments become outdated.
- Increased awareness of links between personal preferences, social goals and technological developments.

Concluding remarks

TA accompanying TT would not only benefit the scientists, who would gain an increased awareness of the societal implications of their research, but also legislators, regulators and policy makers, who will need to be competent on the ethical and legal dimensions of scientific applications. In addition, the debate on genetic engineering has served as a reminder that citizens would like to have their voices heard regarding technology evaluation. The access to accurate, impartial information, that is the result of TA processes, is crucial for policy formulation and societal anchoring of technology development, which are fundamental prerequisites for successful TT.

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Transgenic Plants and Risk Assessment

"In the end, it is human choice and not the content of science that determines the outcome. The content of science can only enhance or potentiate choices rooted in social and ethical values."

Stephen Jay Gould

The Endorsed Risk Assessment Model

Risk assessment, as endorsed by the National Research Council in 1983, consists of four stages: 1)hazard identification; 2)consequence estimation; 3)failure frequency estimation; and 4)calculation of the resultant risk level. When the technical system functions in a closed loop, with a chemical substance or organism, the quantitative and probabilistic risk assessment is based on the identifiable and intrinsic hazard, which might be chemical toxicity, flammability, or the pathogenicity of a cultured organism. This approach is technocratic in philosophy and emphasizes the numerical calculation of risk as the solution to arbitrary and "irrational" risk policy decisions. Fact and value are carefully separated.

Genetically Modified Organism in the Environment: A Participatory Risk Assessment

When the debate on the use of genetically modified organisms (GMOs) erupted in the public arena, it became evident that there was a need for both technical expertise and value choices in the overall assessment of risk. The language of the technical risk assessment, that was applied to the analysis of closed systems, was no longer adequate for dealing with the potential adverse effects of GMO deliberate releases. In most cases, the GMOs being introduced into the environment are modified versions of familiar organisms with a long history of safe use and are expected to have no direct adverse effects for human health or the environment. In comparison with chemical substances or pathogenic organisms in contained systems, the properties of GMOs are not intrinsically hazardous. The damage potential from the introduction of GMOs is related to the interaction of the introduced genetic information, such as herbicide tolerance or insect resistance, with the environment and the potential for the protein product of the introduced gene to be toxic or allergenic for humans. In open applications, GMOs can reproduce in the environment, and the risk assessment should therefore also address the dimension of time in determining the long-term damage potential from their widespread application.

What the discussion on GMOs has achieved, however, is a new consciousness on how we view the environment and our relationship to it. There has been a definite paradigm shift, whereby agricultural systems are no longer accepted as such, but are seen as also affecting the ecological environment surrounding the agricultural landscape. This same distance that was once perceived as normal and necessary for the isolation of two distinct genotypes of the same cultivated crop is now seen, in the light of the GMO discussion, as inadequate for the acceptable range of transgenic pollen flow.

Since the implications of a risk assessment of GMOs are dependent on the social context, a participatory approach is needed to determine the balance of benefits to risks. In addition to the measurable parameters such as the crop performance, yield, fitness, invasiveness, rate of hybridization, the expanded risk equation now also includes non-quantifiable terms such as consumer choice, long-term agricultural policy, ethics and societal responsibility to future generations. One could begin by determining the key stakeholders by asking the following questions: 1)who or what is at risk? 2)who or what do we want to protect? 3)what outcomes do we want? Stakeholders include, among others:

- the farmer, who would like to have a secure income and a market for his products;

- the consumer, who would like to exercise choice and be reassured of the nutritiousness and safety of his food
- the environment and the preservation of biodiversity
- the nation, that desires a healthy economy, a safe and secure food supply and political stability.

Making the Decision Basis Transparent

Science can help to make the decision basis transparent and provide some insight on the quality of the assumptions made in arriving at conclusions during a risk assessment. The same techniques of molecular biology that are used to transform plants with agronomically useful traits have helped us to acquire an increased understanding of natural mechanisms involved in gene transfer, gene acquisition and genetic variability. By understanding the nature of genetic modifications in traditional breeding, the nature of genomic plasticity in plants for intended and unintended effects, it would be possible to determine an accepted safety baseline, against which the safety of the genetic engineering of plants can be evaluated. In the determination of this baseline, data on the impact of gene-environment interactions would be needed to assess the risk of GMO deliberate releases, in addition to an evaluation on the desirability of current practice.

Science can provide the objective "values" that are needed by non-scientific stakeholders, to build the foundation for decisions and policies that will allow the genetic engineering of plants to be an effective way to meet the challenge of producing agricultural products in a rapidly evolving society and changing environment.

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are conducive to investment in biotechnology.

Computerized Decision Support Systems for Risk Assessment

The paper presents the development of a computerised "decision support" system for assessing risks arising from the use of genetically modified organisms (GMOs).

The development of such system is of particular relevance to developing countries where capacity and resources to exercise regulatory oversight are severely limited in most cases.

Existing international guidelines for risk assessment provide a useful starting point but are far too generic and of limited use in "real" situations where researchers and regulators are required to consider risks pertaining to specific organism / genetic modification / environment combinations. Furthermore, risk assessment has to be placed in the context of national and international statutory requirements.

The system provides a tool to preserve, disseminate and interpret available data and information regarding specific organism/transgene/environment combinations. It also serves to enhance familiarity with environmental introductions of GMOs and provide information support to researchers and biosafety reviewers of regulatory authorities and commercial enterprises.

The model system provides a basic methodology of analysing safety issues related to the biology of initially three (3) crop plants, namely, rice, potato and brassica and on three (3) selected traits, namely, virus resistance through the use of viral coat protein genes and insect resistance through the expression of *Bacillus thurigiensis* toxin gene and herbicide tolerance (glyphosate and phosphinothricin).
The system is designed to serve the needs of biosafety officers of government regulatory authorities, and private enterprises as well as of researchers involved in the development and handling of GMOs.

The system is currently operational as alpha version. It is being tested by a number of experts. It is updated and modified virtually on a daily basis. Internet access is also enabled <**http:/binas.unido.org/dt>.** Feedback to-date has been extremely positive and points to directions of further system development.

System design

The decision tree is presented as a series of statements constituting a decision tree type of risk assessment. Statements correspond to putative hazards imposed by the transformation method, the biology of the host organism, the agricultural practice, and the interactions of the GMO with the environment into which it has been released. These statements correspond to indicative statutory information required by regulatory authorities. Selection of statements produces inferences/outputs pointing to actions for risk reduction or risk management and/or need for additional research/testing to compensate for data/information gaps.

It is assumed that, in selecting specific statements, users are guided by information available to them. Ability to select and correctly interpret the statements presented implies multidisciplinary expertise in biology, breeding systems and agro-ecology. Users are assisted by extensive on-line help documentation stored in flat-file databases.

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Genetically Engineered Crops:
How Could We Overcome the Present Day Obstacles in Europe ?

Keywords: Risk Assessment, Regulation, Planning Methods, Environment, Organic Farming, Precision Biotechnology

How can we come from the knowledge to the action ?

Some years ago genetically engineered crops would have all be seen as *tame problems* to be solved with some sessions among executives, hand over the plan to professional PR people and they would have solved everything within a few months. It would have just been a matter of presenting some comprehensive scientific data and the solution would be nearly automatically defined.
But unfortunately, planning problems in the field of green biotechnology have now evolved into *wicked problems* with complex structures and no obvious causal chains. These problems cannot be determined totally in a quantitative and scientific way, there are no solutions existing in the sense of definitive and objective answers alone.

Unfortunately, wicked problems have been treated mainly in two directions:

- Through formalised methods which are suitable only for the solution of tame problems.
- Often solutions have been found empirically, with trial and error acceptable solutions can be found, gifted planners often develop good intuition taking into account also socio-economic factors. But deplorably, too often the systems approach working properly for tame problems ends in a fiasco when tackling wicked problems.

Systems approach of the first and second generation

Much hope has been placed in the *systems approach of the first generation*, which certainly had its merits (Nasa missions, toll bridges, defence systems, designing a super crop etc.). Planning goals were "clearly" defined and all decisions where oriented towards these goals.

In general it can be said that the systems approach of the first generation has been followed by an era of disappointment, since it has not yielded what was expected of it: A number of large and complex projects such as urban renewal, improving the environment, tackling the nutrition problems of mankind etc. can only be considered as failures or partial failures such as the "green revolution".
The main reason is the fact, that the classic paradigm of (rational) Science and Technology is not applicable to the problems of open ecological and/or societal systems. It is very important to realise, that problems in biotechnology are not solely problems of Science, but also problems of society. This does not mean that risk assessment should not be Science based, on the contrary. It would be a big mistake to assume that the involvement of open structures in ecology and human society would give cheap excuses to deviate from the path of Science, when it comes to questions of safety and regulation. Or, even worse, to abuse scientific language in order to achieve an ideologically stamped agenda as certain members of the newly grown protest industry are doing.

Professional management tools which are based on a systems approach of the second generation should not be mixed up with *"Future workshops"* with their frequent and inconsiderate use of pin walls when activist groups start their "planning". Rarely those actions have led to sustainable results, too often future-workshops (German *"Zukunftswerkstätten"*) start with a fulminate brain storming and lots of enthusiasm and later on the participants go home to live their normal lives and they tend to forget about their big decisions taken earlier. If the workshops would be properly carried through after Müllert and Jungk, results would be certainly better.
We should also see the difference to *"Collaborative Learning Workshops",* which can be very delightful and thus also successful in the heads and consequently their subsequent decisions, but rarely such events achieve sustainable results either. It is exactly lacking the process of collaborative decision making. It is important to avoid a misunderstanding: Decision making is not in its basic structure a democratic process, it is a process where people genuinely involved are participating. To be even more explicit: Partners taking part in the decision making process should have their own and genuine interest in the cause, this avoids the danger of manipulation through clever PR, through populist and, even worse, fundamentalist argumentation.
Consensus conferences and also *citizens conferences* are extremely helpful in cases of conflicts in the Public, but here again it is difficult to see that processes criticised will be changed to the better and negative trends are definitively turned around. Lets face the difficulties: How on earth can you expect a citizens group to learn about the complexity of solutions necessary within a few days of intensive briefing ?
Another kind of internal consensus conference is designed by the promoters of the "Syntegrity approach", which brings together corporate people in order to analyse internal dynamics and processes and to discern negative effects.

Despite the fact that there is a lot of effort becoming evident to design new planning and management methods negative results are predominant and are in fact part of a planning crisis, stemming from the seventies and which is still continuing today.

What is the "Systems approach of the second generation" ?

Still, it is primarily the paradox of rationality which has been severely underestimated in the systems approach of the first generation.
The more questions we are asking the more answers are possible and vice versa. Limitations of technological solutions are always hidden in the open ecological and social systems: Just compare the infamous case of DDT sprayings in the past. Constraints in possible secondary effects in ecology should be examined carefully: This is well demonstrated in the case of the

Monarch larvae being killed by Bt-Maize-Pollen, the result of a highly sophisticated laboratory study where press interpretation got way out of proportion – even though the author himself warned about this. Would one have asked the farmers, they would have been able to say that feeding time of the young larvae do rarely overlap with the time of pollen shed of maize, and that the plants the Monarchs are feeding upon are fiercely fought as a weed.

- In order to tackle with wicked problems you need to go through *an extensive process of argumentation*, also called objectification, not to be mixed up with an "objective approach" to the problem.

There is rational planning, but there is no way to start to be rational, one should always start a step earlier, since there are important trends and facts which will make straightforward rational thinking and acting in solving wicked problems useless. It is not the theory component, but rather the political component of the knowledge, which determines the vector of the action. This is the *zero step* so important in the publications of Horst Rittel. This is also the basis of the understanding of the term "*Symmetry of Ignorance"*.
As an example: The fact, that experts can be wrong and farmers know better in certain situations in agriculture because they are better observers out in the field.

The knowledge needed in wicked planning problems is not concentrated in a single head. It is absolutely essential to let all partners be involved in the problem solution process, which includes part of the population (mainly farmers organisations and consumer organisations), the Governmental Regulators, the Non-Governmental Organisations, the Life Science Companies and the Scientists. There is no monopoly of knowledge. Having illustrated the difficulties in solving wicked problems, we need a new approach in problem solving, in order to avoid the pitfalls of ignoring bottom up feedback's.
You only can keep to this rule if you are also following another important rule: All partners in the planning process have to avoid hidden agendas, which is certainly eased by a minimum amount of respect paid to eachother partner. Nobody should be criticised for speaking up in its own interest.

It is obvious in these times of growing difficulties in communicating biotech products, specially in agriculture, that all partners still have a lot of homework to do.

- The Biotech Companies are populated with people who are convinced about their own products, since they now precisely about safety standards and regulatory processes. So far so good, but these people live in a World of euphemisms and perfection, they develop with time a lack of understanding criticism from outside.
- The scientists often are naïve enough to stick to factual, instrumental and explanatory knowledge alone. Many miss a very important point as Hannah Arendt put it: One of the most noble tasks of scientists is to make out of facts Public opinion.
- The regulators should find ways and means to cope up with the growing speed of new developments. One of the main reasons why things in Europe turns sour is the fact that European regulation is way behind the one of the United States. On the other hand, this is an excellent occasion to see more clearly the geographical differences in the regulation.
- Some of the NGO's have developed into powerful protest industries and are not interested in a thorough scientific analysis, since this could blur populist argumentation, which they need to keep up in order to get more donors, which are in fact their shareholders.

- The Public is often lost between the two camps and, surprisingly enough, only a minority feels the need for better education, whatever this would mean according to the two camps described above.

How to Solve Wicked Problems in Biotechnology and the Environment

What we need in such cases is an action oriented approach. Risk Assessment and Management must be seen as a planning strategy of the second generation in developing a professional framework for *decision making*.
Strategies have to be developed to recognise the consequences of our doing on one side, and to specify our knowledge on the other side. This knowledge has to be gained step by step and case by case: If we want to clearly distinguish our present state knowledge from appropriate decisions to be made *not* based on our views and opinions, we need to go through the following steps.

- What is the problem ?
- What do we want ?
- What are the alternatives ?
- How do we compare them ?
- How can we reach the solution ?

All participants need to keep in mind that there are *various types of planning knowledge* (arranged according to the 5 questions asked above):
Examples given here are lumped together as simple keyword-illustrations, taken out of their context in real planning examples, they cannot be regarded as an example of a realistic situation, this would be exactly the task of a planning process of the second generation.

- *Factual knowledge* is the knowledge of what actually happens (quantitative data or empirical, observational data).
  Gene flow species by species / region by region / facts about insect resistance in agriculture.

- *Deontic Knowledge*, the very important knowledge of what ought to be.
  The knowledge about new crops which enhance agricultural production / new agricultural techniques to avoid erosion / new biological approaches to fight insect pests etc.

- *Explanatory Knowledge* explains why things are so or why certain effects will happen. Here already you start to determine the direction of the solution.
  The way Bt proteins are acting on specific pest and beneficial insects / what are the main reasons of unwelcome erosion effects / mechanisms of vertical gene flow / mechanisms of resistance development.

- *Instrumental knowledge* on how to steer certain processes, on how to achieve certain goals, knowledge which needs to be balanced against regulation and safety.
  The way how to build Bt and other genes into crops and how to stabilise them / how to avoid vertical gene flow / how to avoid unwelcome soil erosion / how to avoid early upcoming pest resistance.

- *Conceptual knowledge* which would allow to avoid conflicts before they pop up. This is the knowledge about complex situations, taking into account all previous kinds of knowledge and also weighting them against arguments coming from open ecological and societal systems.

  Concepts about transgenic crops compatible to the ideas of a sustainable agriculture.

You need to go through an *extensive process of argumentation*, also called objectification, not to be mixed up with an "objective approach" to the problem. The hopes of this process are:

- to forget less, to raise the right issue
- to look at the planning process as a sequence of events
- to stimulate doubt by raising questions, to avoid short-sighted explicitness
- to control the delegation of judgement: Experts have no absolute power, scientific knowledge is always limited.

There is no scientific planning.
Solving practical problems as to develop sustainable transgenic crops cannot be dealt with by "scientification of planning". Dealing with wicked problems is always political because of its deontic premises (means that you have to involve knowledge what ought to be). Science only generates factual, instrumental and in the best case explanatory knowledge.
The planner (here the manager of an action plan) is not primarily an expert, but a *"mid-wife of problem solving,* a teacher more than a doctor. Moderate optimism and careful, seasoned respectlessness, casting doubt is a virtue, not a disadvantage of an action plan manager.
The planning process of wicked problems has to be understood as an *argumentative process*, it should be seen as a venture (or even adventure) within a conspirative framework, where one cannot anticipate all the consequences of plans.
Systems methods of the *second generation* are trying to make this deliberation explicit, to support it and to find means in order to make this process more powerful and to get it under better control *for all participants.*

Outlook

It is beyond logic and present day knowledge to predict some surprising outcomes in genetic engineering debates designed as above. Still there are some dreams and hints, which should be placed at the end of this contribution:

"Precision Biotechnology" could lead to a better design of crop seeds in future. Precision biotechnology would mean that a bag of seeds contains a great variety of different kinds of seeds related to resistance against many pest insects on one side, but all having a precisely designed genome for the product quality to be sold after harvest. Genomic research offers a great future and will greatly speed up modern breeding and add considerably to its precision. Here we also find the key of reintroducing some old concepts of getting modern agriculture closer to biodiversity again.

Organic farming needs in future go together with modern breeding methods including genetic engineering. This is in the eyes of the authors an absolute need but also a very difficult thing to achieve, since the transgenic crops of the first generation are either not made for the strategies of organic farming or even worse, they work against such visionary strategies.

Maybe we need some newly designed products which will fit to terms like *Organo-Transgenic Crops* and *Organic Precision Biotechnology ?*

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Ecological Studies of Gene Flow to Weedy Relatives of Crops

Gene flow between crops and wild plants is often cited as an undesirable consequence of adopting transgenic crops. Gene flow occurs when pollen moves from a crop to a wild relative – or *vice versa* – and genes from their offspring spread *via* the dispersal of pollen and seeds. Crops and weeds have exchanged genes for centuries, so this process is not new. Now, however, it is possible use genetic engineering to select useful genes from viruses, bacteria, insects, and vertebrates, as well as related or unrelated plants, and transfer these genes to crops. Therefore, the types of genes that can spread to weeds are much broader and potentially much more effective than genes from conventional breeding. A fundamental question, then, is what impact could transgenes have on the abundance and distribution of weeds? Should we be concerned about weeds that gain resistance to insects, diseases, harsh conditions, and commonly used herbicides?

To begin to answer this question, we need to determine which crops hybridize spontaneously with wild/weedy relatives in a given country or region. Using examples from North America and Europe, I will describe studies showing that crop genes can persist for many generations in wild populations, even when first-generation crop-wild hybrids have lower fitness than wild plants. In cases such as sunflower, squash, and radish, the crop and the weed are different forms of the same species, and crop-to-wild gene flow occurs whenever these forms grow near each other. Gene flow can also occur when crops and weeds are more distantly related, for example between wheat (*Triticum aestivum*) and jointed goatgrass (*Aegilops cylindrica*), sorghum (*Sorghum bicolor*) and johnsongrass (*Sorghum halepense*), or oilseed rape (*Brassica napus*) and field mustard (*Brassica rapa*). On the other hand, gene flow from maize, cotton, soybean, potato, and many other species is not a problem in the USA or Europe because wild or weedy relatives of these crops do not occur nearby. Thus, the extent of gene flow between crops and weeds should be examined on a case-by-case basis in different geographic regions.

Currently, it is not possible to prevent gene flow between sexually compatible species that hybridize spontaneously. Therefore, it is important to determine which types of transgenic crops have novel traits that might be beneficial to wild or weedy relatives. In the short term, the the spread of transgenic herbicide resistance may create logistical and/or economic problems for farmers. For example, transgenes that confer resistance to glyphosate (Round-Up) or glufosinate (Basta, Liberty) are expected to spread to weedy crop relatives that could otherwise be controlled by these commonly used herbicides, thereby requiring applications of multiple types of alternative herbicides. Herbicide resistance could also spread to other plantings of the crop and to volunteer or feral crop plants. Delaying increases in populations of herbicide-resistant plants should be a basic goal of sustainable agricultural practices.

Over the longer term, certain weeds are likely to benefit from transgenes that confer resistance to ecological factors such as herbivores, diseases, or harsh growing conditions. Initially, the effects of one or a few transgenes may be difficult to detect unless weed populations are released from a strongly limiting factor (e.g., drought stress). For most weeds, we do not know the extent to which various ecological factors limit the weed's abundance, competitive ability, or geographic range. With limited knowledge, ecologists are not able to predict whether transgenic weeds could become more difficult to control. Nonetheless, ecological research can provide helpful information for risk assessment. For each type of transgenic crop, one could ask the following questions:

1) Will the transgene(s) spread to free-living populations that are weeds in agricultural or natural areas?

2) If so, are the transgenes likely to enhance the survival or seed production of weedy relatives?

3) If so, could the proliferation of such transgenic weeds lead to serious economic or environmental problems?

4) If so, are these risks outweighed by the expected benefits of adopting particular types of transgenic crops, or should the release of these crops be prevented?

In conclusion, I would like to mention several misperceptions about crop-to-wild gene flow that have been promulgated by the media and others. Many people erroneously think that *all* gene flow from transgenic crops to wild plants is dangerous. Some even believe that crop genes can spread to *any* weed species, or that "Terminator" genes could spread through wild populations to cause massive die-offs. Another concern is that transgenes could "pollute" the gene pools of endangered plant species. Many endangered species are indeed threatened by habitat loss and/or hybridization with cultivated plants, but this occurs with conventional agriculture as well. Transgenic crops represent a powerful and profitable extension of conventional breeding methods. A challenge for the future will be to use this technology wisely, as part of a long-term strategy to improve human health, preserve biodiversity, and promote more sustainable agricultural practices.

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Long-Term Monitoring of Transgenic Crops (Powerpoint Presentation)

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Vitamin-A and Iron-Enriched Rices May Hold Key to Combating Blindness and Malnutrition: A Biotechnology Advance

The major micronutrient deficiencies worldwide concern iron, with 24% of the world's population (up to 60% in developing countries) or 1.4 billion women suffering from iron deficiency, anemia, and vitamin A with up to 800 million children, or 14% of the world population. The deficiencies are especially severe in developing countries were the major food staple is rice. To contribute to a solution of the problem we set out to genetically engineer rice toward an improvement in the supply of vitamin A and iron.

Iron deficiency caused from rice diets is the consequence of a) low amounts of iron in the endosperm, b) high concentration of phytate (the major inhibitor of iron resorption in the intestine), and c) lack of sulfur containing proteins enhancing iron resorption. Consequently, we aimed at a) an increase in iron content via a ferritin transgene from Phaseolus vulgare, b) the reduction of phytate in the cooked diet via a transgene for a thermotolerant phytase from Asspergillus fumigatus, and c) at the overexpression of a cystein-rich metallothionin-like protein from Oryza sativa. All genes were under endosperm-specific control. The transgenic rice plants, so far (in the segregating first sexual offspring) , show a two-fold increase in iron, high activity of the phytase (digesting phytate completely in a simulated small intestine experiment), and an increase in the cystein content of ca. 25%.

Rice endosperm does not contain any provitamin A. The latest precursor to the pathway is GGPP. Theoretically, four enzymes should complete the pathway towards provitamin A. These are phytoene synthase, phytoene desaturase, zeta-carotene desaturase, and lycopene cyclase. The necessary genes for these enzymes have been isolated from Narcissus (daffodil). They could be complemented by a double-desaturase from the bacterium Erwinia uredovora, catalysing both desaturation steps. Transgenic rice plants carrying the genes in combination produced seeds with yellow endosperm. Biochemical analysis confirmed that the colour was due to the presence of such amounts of provitamin A, that its content in a typical Asian rice diet (300 g of uncooked rice) alone would provide the necessary daily dose of vitamin A to prevent vitamin A-deficiency.

Both vitamin A and iron are combined by crossing. The material is transferred free of charge and any restrictions for non-commercial use to developing countries. Arrangements with rice breeders for crossbreeding to local varieties have been initiated for the major rice growing countries in Asia, Africa and Latin America.

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Indian Rules, Regulations and Procedures for Handling Transgenic Plants

The Indian Government had promulgated the Rules for dealing with Genetically Modified Organisms (GMOs) in 1989. The GMOs include the products of GMOs as well. The Rules define constitution and functions of competent authorities. They also elaborate the implementation structures for conducting research and for the commercial applications of GMOs. The research on GMOs is monitored by the Review Committee on Genetic

Manipulation (RCGM) which stewards the generation of biosafety data starting from lab to contained green house experiments to small scale contained field trials. The biosafety data required to be generated include the rationale for the development of GMOs, details of their molecular biology, comparison of germination rates, phenotypic characteristics, study of gene flow, invasiveness and weed formation possibilities, susceptibility to diseases and pests, effect on non-target organisms and food safety evaluation. The agronomic evaluation is also conducted. RCGM also authorizes the import/ export/ transfer of transgenic genetic materials for research use only. The Genetic Engineering Approval Committee (GEAC) provides authorization of GMOs for commercial release based on biosafety evaluation data. The major Indian developments in transgenic plants include work on transgenic cotton, Indian mustard/oil seed rape, tomato, brinjal, cauliflower, cabbage, potato, tobacco, chili, bell pepper and rice.

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Plant Genetic Engineering in India

More than 80% of India's population is involved in agriculture and its supporting activities. Increasing crop productivity has always been a majo agenda in Indian planning. Intense plant breeding programmes in many Agricultural Universities and other public and private research centres immensely contributed to successful 'Green Revolution' in India. The importance of genetic engineering in increasing crop productivity to a higher order is well recognized in India. Public and private sectors have taken many efforts in the past ten years to prepare the Indian research base for the deployment of genetic engineering strategies for crop improvement.

The Department of Biotechnology (DBT), an organ of the Ministry of Science and Technology, Govt. of India, recognised the importance of establishment of research infrastructure and development of scientific manpower in Plant Molecular Biology. In that direction, seven Centres of Plant Molecular Biology were established in different parts of the country during the past ten years. Recently, a Plant Genome Research Centre has also been established in New Delhi. Many National Research Facilities in Genetic Engineering and Bioinformatics Centres established in different locations provide the required additional research support. Postgraduate courses in Biotechnology and many Diploma courses in Biotechnology taught in many centres with the financial support of DBT provide well-trained scientific manpower for Plant Genetic Engineering.

Government-funded genetic engineering research programmes are highly focussed to the major Indian crops such as wheat, rice, Brassica, cotton, chickpea, and other important pulses. Selected high priority genetic engineering programmes on the development of resistance to cotton pests, cotton leaf curl virus, rice tungro virus, mungbean yellow mosaic virus and tomato leaf curl virus have recently been initiated at multi-institutional level. Rice plants expressing synthetic cryIAc and eggplants expressing cryIAb are ready for limited field evaluation.

To guide genetic engineering research in an environment-friendly direction, the Department of Biotechnology has evolved detailed Recombinant DNA Guidelines in 1990. The Government has also evolved a good Institutional mechanism for effectively implementing the Safety Guidelines. With the adequate research infrastructure already established and with well trained scientific manpower, India is poised to exploit plant genetic engineering to solve many of its problems related to crop improvement.

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Indian wheat program

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Development, Testing and Commercialization of Transgenic Papaya in Hawaii

Papaya (*Carica papaya*) is Hawaii's second most important fruit crop behind pineapple, with both fruits being symbolized as the type of delicious fruits that are grown in Hawaii. The Hawaiian solo papaya is the dominant papaya that is grown in Hawaii; it is small, averaging about one pound, sweet, and have good shipping qualities. The commercial market of Hawaii's papaya includes mainland USA, Japan, and Canada. The industry's main cultivar is 'Kapoho,' a yellow-flesh papaya that is adapted to the volcanic and rainfall conditions of Puna on Hawaii island. The red-flesh 'Sunrise' and 'Sunset' are also grown but in far lesser quantities then 'Kapoho.' Papaya throughout the world is affected by papaya ringspot virus (PRSV), a potyvirus that is transmitted by aphids. Resistance to PRSV has not been found in papaya. PRSV was reported in Hawaii in the 1940s. It eliminated wide-scale commercial papaya production on Oahu island in the 1950s and caused the industry to move to the Puna district on Hawaii island, where there was no PRSV. By the late 1960s, 95% of Hawaii's papaya were being grown in Puna. However, PRSV was a potential threat because it was in an area about 19 miles from the Puna district. In 1987, a group of researchers started a project to develop transgenic papaya for Hawaii using the pathogen-derived resistance approach where the coat protein gene of the virus is transformed into the papaya. The main research group included Drs. Jerry Slightom from the former Upjohn Company, Dr. Richard Manshardt from University Hawaii, Dr. Maureen Fitch who was then a graduate student under Richard Manshardt, and Dennis Gonsalves. Sunset papaya was transformed with the coat protein gene of PRSV-HA 5-1 isolate from Hawaii by bombarding embryogenic calli with a plasmid containing the coat protein gene and other elements used for selection and gene expression. By 1991, greenhouse tests identified a PRSV resistant transgenic line, which was designated 55-1. An APHIS (Animal Plant Health Inspection Service) permit for a field trial was obtained, and small trial of less then 40 R0 propagants of line 55-1 was established on Oahu island on April 1992. By December 1992, the results clearly showed that line 55-1 was resistant to PRSV under field conditions. As fate might have it, the long awaited invasion of PRSV into the papaya fields of Puna was detected in May 1992. Unfortunately, by the end of 1994 PRSV was widespread in Puna and the papaya industry was in serious trouble. The transgenic papaya project changed from academic research status to a possible solution for helping the Hawaiian papaya industry. The long term continuation of the 1992 field trial also proved valuable since it allowed for the development of two virus resistant cultivars. One was the red-flesh 'SunUp' which is line 55-1 that is homozygous for the CP gene and the other was the yellow-flesh 'Rainbow' which is the F1 hybrid generated by crossing 'SunUp' and the nontransgenic 'Kapoho.' Under permit from APHIS, a large-scale field trial consisting of over 800 test plants was established in October 1995 in a farm in

Puna that was severely affected by PRSV. Dr. Steve Ferreira of the University of Hawaii joined the group to head up the field trial. The Puna field trial conclusively showed that 'SunUp' and 'Rainbow' being grown under farm conditions were resistant to PRSV. Growers and packers were made aware of our activities and got to personally see the transgenic field trial. 'SunUp' and 'Rainbow' proved to be highly acceptable cultivars, as judged by farmers, packers, and consumers. During the course of the trial, petitions were submitted to APHIS and EPA (Environmental Protection Agency) to obtain deregulatory status for the transgenic papaya. These were obtained in 1996 and 1997. The consultative process with FDA (Food and Drugs Administration) was completed in September 1997. Since the transgenic papaya was developed using various materials and processes that are covered by intellectual property rights, licenses to these rights had to be obtained before the product could be commercialized. The PAC (papaya administrative committee) took up the task of obtaining the necessary licenses. PAC is a group of papaya producers and handlers that voluntarily formed a USDA (United Stated Department of Agriculture) marketing order to help solve problems of marketing papaya. All licenses for the intellectual property rights were obtained in April 1998. Distributions of 'SunUp' and 'Rainbow' seeds to growers were started on May 1, 1998. Many acres of once abandoned papaya fields in Puna are being reclaimed by transgenic papaya. As of November 1999, the papaya are showing excellent resistance and fruit are being sold in the US markets. This papaya case points out how the efforts by researchers, regulatory agencies, growers, and producers helped Hawaii maintain good production of Hawaiian solo papaya for which it has been long associated.

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Impact of Transgenic Papayas on the Hawaii Papaya Industry

On the eve of May 1st, 1998 Hawaii papaya farmers rejoiced as they gathered together for a *luau* feast at the Hilo Hawaiian Hotel along the shores of Hilo Bay. They were celebrating the debut of the newly commercialized virus-resistant 'Rainbow' and 'SunUp' cultivars -– their hope for a brighter future.

Celebrants included many personnel who had labored to help the farmers during their battle against papaya ringspot virus (PRSV). These included researchers and extension agents from the University of Hawaii, workers from the Hawaii Department of Agriculture and from the

United States Department of Agriculture, among others. The evening began with prayers, Hawaiian chanting, and a bedecked procession which included papaya industry representatives and other supporters, as well as the inventors of 'Rainbow' and 'SunUp'.

In Hawaii, PRSV was first discovered in the 1940's on the island of Oahu, causing the papaya industry to move to the island of Hawaii during the 1950's. By 1992, farmers were producing 95% of Hawaii's papayas in the virus-free Puna area on the island of Hawaii. But unfortunately, PRSV entered this area in 1992. Within five years the virus had caused major losses, and efforts to control PRSV by rouging were abandoned.

By 1998, papaya production had fallen an estimated 25% and was continuing to decline. More strikingly, Kapoho, in the Puna District suffered a major 100% loss in production when all of its 800 acres of papaya trees succumbed to the virus. This loss represented one-third of the papaya acreage on the island of Hawaii.

Fortunately, long before the onslaught of the virus, efforts were underway to impart pathogen-derived resistance into papaya. 'Rainbow' and 'SunUp' were developed and became the first virus-resistant transgenic fruit to be commercialized in the United States. Many important questions on health, safety and environmental impact were addressed during the deregulation phase.

But now, what about the farmers? What are the factors "for" or "against" their adoption of these new cultivars? What are their concerns about genetically modified papayas? What do they think about labeling? Are the transgenic fruit any good? Are the trees productive? Are there any problems in growing the transgenic papayas? Have these new cultivars enabled economic benefit? Have these cultivars improved their lives in other ways? Currently, all the seeds were given to the farmers free of charge. If it is necessary to sell the transgenic seeds in the future, are they willing to pay?

This presentation will discuss the methodology and results of personal interviews with 100 papaya farmers in the Puna area of Hawaii. Over 90% of the farmers are Filipinos, and many of them are first generation immigrants to the United States. In some respects they represent a "developing" culture, and some of their experiences can be useful in considering impact and technology transfer of transgenic plants to farmers in developing countries. How can we ensure a lasting celebration long after the debut is over?

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Introducing Transgenic Products into Developing Countries

Papaya (*Carica papaya*) is grown in backyards of homeowners, by small subsistence farmers, and by large commercial growers throughout tropical and subtropical lowlands. Papaya ringspot virus (PRSV) causes the most important viral disease of papaya. Control of PRSV is difficult because it is transmitted by aphids and natural resistance has not been found in papaya. The development of PRSV resistant transgenic papaya for Hawaii spurred interest from developing countries to obtain virus resistant transgenic papaya for their country. As a result, my laboratory has worked with the Cornell Research Foundation, which handles intellectual property rights matters for the university, on a program for the safe, timely, and cost effective development and introduction of transgenic papaya to developing countries. The general approach involves matriculation of a scientist (or graduate student) from the developing country to my laboratory for learning and applying the skills that are necessary for developing transgenic papaya that are resistant to PRSV in their country. The target time period for the visiting scientist to develop the transgenic papaya is around 18 months and naturally longer for a graduate student. This relatively short time period is possible because of the presence of people in the laboratory who are able to help the scientist and because efforts are made to have embryogenic calli started early in the project. At an early stage, Cornell Research Foundation discusses the intellectual property rights with the proper personnel from the country. A mutually beneficial agreement is essential if the product is to be commercialized in the country. Initially, transgenic papaya developed by the scientist are tested in my laboratory against a strain of the PRSV from the target country to identify potential resistant lines. Also, before papaya is sent to or taken back to the developing country, the scientist works with their government in satisfying all criteria for introducing the transgenic papaya. Once in the country, the scientist and other personnel would follow the biosafety protocols for greenhouse and field testing to evaluate the suitability of the product. So far, the program has resulted in the development of transgenic papaya for Thailand, Jamaica, Venezuela, and Brazil. The papaya are at various stages of testing: from field trials in Jamaica and Thailand to being in quarantine in Brazil. Various aspects and challenges facing this approach will be discussed.

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Legal Perspectives on the Transgenic Papaya Licensing Program

In the fall of 1995, I was retained by papaya growers in Hawaii to provide legal assistance on patent and licensing issues relating to a transgenic, disease-resistant papaya which had been developed for use in Hawaii. Although this technology was developed by Dennis Gonsalves of Cornell University as well as researchers in Hawaii, my client was actually the Papaya Administrative Committee ("PAC") in Hilo, Hawaii. PAC was created under a Federal Marketing Order by the U.S. Department of Agriculture to assist the Hawaiian papaya industry in marketing papaya. However, as a result of the devastating effect of papaya ringspot virus on the industry, PAC undertook to obtain the patent licenses necessary for commercial introduction of the transgenic, disease-resistant papaya.

As PAC's legal advisor, I was required to identify what patent rights needed to be licensed, to negotiate and obtain licenses, and to help PAC administer the licenses which were obtained. This paper describes how I assisted PAC in these respects as well some practical considerations relating to the patenting and licensing of transgenic plant technology.

I. Identification of Patent Rights Which Needed to be Licensed

Under 35 U.S.C. § 271, a U.S. patent gives its owner the right to prevent others from making, using, selling, or offering to sell the subject matter of the patent in the United States. The recipient of a license of such patent rights has the ability to engage in at least some of these activities without risk of either being subject to an injunction preventing use of the technology and/or liable for damages. PAC wanted to be able to go forward quickly with the transgenic papaya without such risks. Therefore, my first task was to determine what patent rights needed to be licensed by PAC.

Deciding what patent rights needed to be licensed involved determining what patents would be infringed by the transgenic papaya technology in the absence of a license. In order to proceed, it was first necessary to identify what technology was used in making the transgenic papaya. Based on this information, a group of patents which potentially needed to be licensed were identified. Such identification of candidate patents often requires conducting an infringement search on computer databases and in the U.S. Patent and Trademark Office

("PTO"). In the case of transgenic papaya, we also had some guidance from industry sources. Once a group of candidate patents was identified, I proceeded with the legal analysis of which of those patents would actually be infringed.

The exclusionary rights afforded by a U.S. patent are defined by the claims. Therefore, in analyzing a patent for infringement, it is first necessary to interpret the scope of the patent (i.e. the claims of the patent).[1] This involves examining the literal language of the claims, reviewing the specification (i.e. the body) of the patent, and studying the prosecution history of the corresponding patent application (i.e. the correspondence to and from the PTO during the patent application process).[2] Through this analysis, the meaning of the terms in the patent claims and, accordingly, the scope of the claims as a whole is determined. With this information, it can then be determined whether the claims are infringed by the subject technology.[3]

A U.S. patent can be directly infringed in two ways—i.e. by literal infringement or under the doctrine of equivalents.[4] Literal infringement occurs if the language of the claims literally covers the subject technology.[5] The absence of literal infringement does not, however, mean that infringement is avoided. There can still be infringement under the doctrine of equivalents if the differences between the subject technology and the claimed invention are insubstantial.[6] One approach to determining whether there is infringement under the doctrine of equivalents is to analyze whether the subject technology and the patented invention do substantially the same thing in substantially the same way to achieve substantially the same results.[7] The scope of the doctrine of equivalents is limited by what the prior art teaches and by what the patentee surrendered during prosecution of the patent.[8]

The technology used by Dennis Gonsalves and colleagues to develop a transgenic papaya is described in Ling et al., "Protection Against Detrimental Effects of Potyvirus Infection in

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[1] Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 219 USPQ 1137 (Fed. Cir. 1983).

[2] McGill, Inc. v. John Zink Co., 736 F.2d 666, 672-75, 221 USPQ 944, 948-50 (Fed. Cir.), cert. denied, 469 U.S. 1037 (1984).

[3] Fromson v. Advance Offset Plate, Inc., *supra*.

[4] Radio Steel & Mfg. Co. v. MTD Products, Inc., 731 F.2d 840, 221 USPQ 657 (Fed. Cir.), cert. denied, 469 U.S. 831 (1984).

[5] Johnston v. IVAC Corp., 885 F.2d 1574, 12 USPQ2d 1382 (Fed. Cir. 1989).

[6] Hilton Davis Chemical Co. v. Warner Jenkinson Co., 62 F.3d 1512, 1521-22, 35 USPQ2d 1641, 1648 (Fed. Cir. 1995), rev'd on different grounds, 520 U.S. 17 (1997).

[7] Id.

[8] Loctite Corp. v. Ultraseal, Ltd., 781 F.2d 861, 228 USPQ 90 (Fed. Cir. 1985).

Transgenic Tobacco Plants Expressing the Papaya Ringspot Virus Coat Protein Gene," Bio/technology, 9:752-58 (1991) and Fitch et al., "Virus Resistant Papaya Plants Derived from Tissues Bombarded with the Coat Protein Gene of Papaya Ringspot Virus," Bio/technology, 10:1466-72 (1992). In brief, they prepared a vector and introduced it into papaya by biolistic transformation. The vector, a map of which is shown in Figure 1, was an *Agrobacterium*-binary vector which included the 35S promoter, the 5' untranslated leader sequence, the papaya ringspot virus coat protein encoding gene, and the GUS gene. Thus, we needed to consider licensing patent rights relating to various DNA components, plant transformation procedures, modes of plant disease resistance mediation, and transgenic plants.

With the assistance of Dennis Gonsalves, I analyzed the technology utilized in developing the transgenic, disease-resistant papaya and determined which of the candidate patents needed to be licensed. In particular, it was determined that licenses were needed from Company Y for patent rights relating to various components of the vector and the general mode of plant disease resistance. From Massachusetts Institute of Technology ("MIT"), we decided to license rights to the 5' untranslated leader sequence. Company X had rights to technology to impart resistance to papaya ringspot virus by use of a gene from the virus. We wanted to license that technology. We also wanted rights to the GUS gene from Cambia Biosystems LLC. On various grounds, we decided that licenses were not needed for other candidate patents.

II. License Negotiations

Having identified which patent rights PAC should license, our next job was to obtain the necessary licenses. This proved to be a very difficult task in view of substantial differences between the strategic objectives of the parties.

PAC wanted to distribute transgenic papaya seed without necessarily charging recipients and without having to maintain the accounting records normally needed for licenses involving a royalty on net sales. Therefore, we sought licenses involving a one-time up-front payment. With this strategy, PAC also wanted to be assured that it would receive licenses under any patents infringed by the transgenic papaya which issued after the license agreement was signed. Otherwise, PAC would be at risk of having to negotiate a new license and making further payments to a party that had already granted a license to PAC. Another issue was PAC's financial resources. Since PAC's licensing activities were financed by public funds and contributions from its members, many of whom were subsistence farmers in Hawaii, the licensing fees needed to be manageable. While PAC needed a substantial level of accommodation from licensors on financial issues, its demands on the scope of any grant under a license agreement were modest. In particular, PAC needed to obtain the right to grow transgenic papaya plants in Hawaii and to sell the resulting fruit worldwide. Finally, since PAC did not itself grow or sell papaya, it needed to be able to sublicense its rights to constituents, including growers.

All of the licensors were sympathetic to the need to introduce a transgenic, disease-resistant papaya in Hawaii. However, they had their own strategic interests which needed to be protected. Some did not, at that time, have a policy of or experience with licensing out and were reluctant to proceed with setting a corporate-wide strategy based on a license for a very small crop. There also was undoubtedly concern with having any deal with PAC dictate what terms would have to be offered for future licenses on strategically important crops. Many of the business development people working for the licensors were very busy and did not have much time to worry about a deal for a very small crop and little economic return. Some licensors had a tremendous commitment to developing a plant biotechnology business and wanted to insure that any licensees of its rights did not jeopardize the industry as a whole. Lastly, the licensors needed to know that the financial terms of any license were fair.

Given the relatively low strategic interest a transgenic papaya license had to the licensors, PAC had to engage in an extensive effort to educate them about the Hawaiian papaya industry, the impact of papaya ringspot virus in Hawaii, and the benefit of the transgenic papaya to papaya growers in Hawaii. In particular, we tried to gain sympathy from the licensors by explaining that the virus had devastated the Hawaiian papaya industry and that the transgenic papaya needed to be introduced in Hawaii to insure that subsistence farmers could maintain their livelihood. This often led to questions about what was PAC and who were its members. When the licensors saw that large, well known fruit packing companies were members of PAC, there were usually questions about who was being aided by the licenses. However, we were able to explain that the true beneficiaries of the licenses were growers whose farms were being severely hurt by the papaya ringspot virus.

In some cases, sympathy for the plight of growers was not sufficient and the licensors needed to be further motivated. The U.S. Department of Agriculture ("USDA") was a big help in several instances. As an important regulatory agency in the plant biotechnology industry, the licensors wanted to remain in USDA's good graces in order to avoid jeopardizing regulatory approvals for their own projects. Since USDA created PAC, was actively involved in the Hawaiian papaya industry, and very much wanted to see the transgenic, disease-resistant papaya introduced in Hawaii, USDA was very willing to help PAC. Without that help, a number of the licenses may never have been obtained.

Once we had communicated with the licensors, we were generally able to persuade them to prepare a draft license agreement upon which license negotiations proceeded. Although we generally prefer to generate the first draft of a license agreement, this tends to be more costly and we were trying limit PAC's costs on this project. In any event, once a draft license agreement was received, we proceeded with license negotiations and ultimately were able to enter into license agreements with all of the targeted licensees.

Company X was anxious to put the transgenic papaya into commerce as a philanthropic effort. It was PAC's first licensor.

Cambia Biosystems LLC is a technology licensing company without any particular interest in itself exploiting the GUS gene technology in the plant biotechnology industry. They were interested in helping the Hawaiian papaya industry as long Cambia could be assured of a fair deal from an economic standpoint. Cambia was our next licensee.

Company Y was sympathetic to the plight of the Hawaiian papaya industry, but as a result of its extensive involvement in the transgenic plant industry had the most difficult strategic interests to harmonize. Once it was able to resolve its objectives, Company Y moved enthusiastically forward with license negotiations. It regarded the license to be negotiated here as a prototype for future deals involving outlicensing of Company Y technology. Company Y became PAC's third licensor.

The last license was obtained from MIT which had no particular strategic concerns about licensing in the plant biotechnology industry but was concerned about whether a paid-up license provided fair compensation. We ultimately were able to develop an arrangement by which MIT could be assured of an economically fair deal.

As a result, PAC had obtained the licenses it needed to begin growing transgenic papaya in Hawaii. Shortly after the last license agreement was executed, PAC began distribution of transgenic papaya seed to growers. The commercial use of this product of biotechnology is expected to have a substantial beneficial economic impact on the Hawaiian papaya industry.

III. Lessons Learned

There are number of lessons which can be learned from the transgenic papaya licensing effort. These lessons, relating to both patent and licensing issues, can benefit researchers, technology transfer professionals, business people, and lawyers.

Researchers in the transgenic biotechnology area should recognize that there are patents covering many commonly-used genetic components and plant transformation procedures. The manufacture, use, or sale of such patented materials by researchers without a research license is an act of direct patent infringement (See Figure 2 attached hereto). This can put the researchers' employers at risk of being sued and having to pay attorney fees and the patentees' damages. If the researcher is employed at an academic institution, the prospect of incurring such expenses is daunting. Even if a research license is obtained, this will not enable introduction of the product of research into a commercial product. Any effort to do so is also an act of patent infringement. In the case of an academic institution working with commercial entities, the licensing out of technology utilizing the patent rights of others or the transfer of materials incorporating patented subject matter also raises issues of patent infringement. In particular, the institution can be deemed to be inducing infringement (i.e. aiding and abetting the infringing acts of another) or engaging in contributory infringement (i.e. selling or offering to sell a material having no substantial use other than in conjunction with a patented process) (See Figures 3-4 attached hereto). To avoid these issues, researchers should use unpatented or easily licensed technology wherever possible.

On the other hand, developers of technology wishing to enhance their licensing royalties and leverage over competitors may wish to make their technology freely available once the necessary patent applications have been filed. The widespread use of such technology can lead to its adoption as an industry standard for which substantial licensing revenue can be derived. Moreover, the use of a company's patented technology in the commercial product of a competitor can give the company significant leverage over the competitor in accessing technology owned by the competitor, maximizing royalty payments from the competitor, and preventing the competitor from introducing an important commercial product.

In licensing patent rights from others, it is important to examine what the various patents that you are considering actually cover. In the transgenic plant industry, there is a great deal of "street talk" about patents and what they purport to cover. Reliance on "scuttlebutt" can result in the procurement of and payment for licenses on patent rights which are not needed. On the other hand, the failure to obtain all the necessary licenses raises the specter of an injunction, liability for damages, and litigations costs. A careful analysis of the patent landscape is well worth the expense.

For entities licensing technology on behalf of others, it is important to properly control how it makes technology available. In the case of PAC, it has made transgenic papaya seed available to growers only after they attend an educational program and sign a material transfer/sublicense agreement with PAC. Similarly, researchers wishing to obtain transgenic papaya seed from PAC need to sign a material transfer/research sublicense agreement with PAC. These measures were undertaken to insure that growers and researchers were knowledgeable about their obligations pursuant to the license agreements and complied with those obligations.

IV. Conclusion

The above events may not be of huge economic significance to worldwide agriculture. However, as one of the first efforts to develop a transgenic fruit crop, procure the necessary licenses, and introduce a product into commerce, Hawaii's transgenic papaya story is certainly an important event for the plant biotechnology industry. The successful results achieved by PAC may well serve as a model for future transgenic plant technology.

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Biosafety Protocol

The Convention on biological diversity was adopted in 1992 at the United Nations Conference on Environment and Development in Rio. This Convention foresees specific measures to be implemented both at the national and international level to achieve safety in biotechnology. In particular, Article 19.3 invites the Parties to the Convention "to consider the need for and modalities of a protocol setting out appropriate procedures including in particular, advance informed agreements in the field of safe transfer, handling and use of any living modified organisms (LMO) resulting from biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity".

In 1995 in Jakarta the 2nd Conference of the Parties to the Convention on Biological Diversity (COP2) came to the conclusion that there was a need for an international legal instrument to address the issue of biosafety. Therefore the COP2 decided to launch a negotiation process to develop a protocol on biosafety specifically focusing on the transboundary movement of living modified organisms. For this purpose the Biosafety Open-Ended Ad Hoc Working Group (BSWG) was established.

The BSWG met six times between 1996 and 1999. In 1998, noting the progress made during the negotiation, the 4th meeting of the Conference of the Parties to the Convention on Biological Diversity (COP4) decided that the protocol would be adopted by an extraordinary Conference of the COP (exCOP) in Cartagena by the beginning of 1999.

Unfortunately, the Cartagena meeting was unsuccessful. No agreement was found and the exCOP was suspended. The main divergences were on one hand the status of the agricultural products containing LMOs and intended for use as food or feed or for processing (commodities) and on the other hand the relationship between the Biosafety Protocol and other international agreements, in particular the WTO. The negotiation will resume and the protocol will hopefully be adopted at the last meeting of the exCOP in Montreal (January 24-28, 2000).

The Biosafety protocol is intended to address the transfer of LMOs from one country to another. The central element of the protocol will be the procedure of Advance Informed Agreement (AIA). AIA will require notification to and consent from the Importing Party previous to the first transfer of a new LMO intended for introduction into the environment. In the opinion of the Miami group (composed of six major grains exporters), LMOs used as food, feed or processing are not intended for introduction into the environment and therefore the AIA procedure must not apply to them. Developing countries are defending the opposite position. One possible solution could be a differentiated procedure which will specifically focus on the needs of developing countries without domestic regulatory framework and which will be based on information provided in advance by countries where the LMO has been put on the market originally.

Apart from the AIA the protocol foresees also provisions on information-sharing, capacity building, risk assessment and risk management, packaging and identification, public awareness and participation as well as more controversial issues on the use of the precautionary principle, socio-economic considerations and liability.

In my presentation I will discuss in detail the provisions of the draft protocol, the current status of the negotiation and the possible implications of the different options under discussion for developing countries.

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Labeling of GMOs and Products Thereof

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Biotechnology Capacity Building

Market failure, In the developing world, is compounded by the absence of technology transfer mediator mechanisms, lack of government regulatory and intellectual property protection properties. These constitute significant disincentives for private investment and innovation in biotechnology. In this regard, the effectiveness of biotechnology to meet domestic needs is crucially dependent upon actions that strengthen the capacity of public and private research systems. Such actions include both the absorption of technological spin-offs that can be adapted to serve domestic needs, and the introduction of policy and institutional reforms that are conducive to investment in biotechnology.

It, therefore, appears to be expedient for developing countries to gear part of their biotechnology research capacity building towards the effective exploitation of existing knowledge, rather than the generation of new knowledge. The use, assimilation and adaptation of new knowledge should be an integral part in the cumulative learning process that would increase a country's potential for upgrading its R&D capability. Clearly, biotechnology R&D alone is not the be all and end all. It is, nonetheless, critical in overcoming some severe bottlenecks of conventional agricultural programmes and enhancing their delivery prospects.

The role of the international agricultural research system in supporting national R&D programmes cannot be overemphasised. However, the situation to date is not promising. International donor and technical support agencies have been reluctant to redirect funds from

conventional types of capacity building and R&D programmes in favour of biotechnology. This is attested by the fact that funding for biotechnology-related R&D is of the order of $30 million per annum. This figure pales in comparison with public sector investment in agricultural research in industrialised countries (Federal US. funding for agricultural research in 1996 was an order of magnitude higher) and is totally eclipsed by private investment.

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Technology Transfer, Biosafety and Intellectual Property Challenges for Sustainable Development

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Perspectives on Transgenic Crops Development and Use in Africa

Introduction

I am very pleased to be in Basel this week to take part in this important meeting and to share with you my thoughts on one of the most debated aspects of biotechnology - transgenic technologies in agriculture. Discussing a subject as complex and controversial as genetically modified crops and their role in the African economies in twenty minutes is a formidable task. I will therefore, only briefly speak about three issues, namely; the compelling needs for these technologies in Africa, the potential benefits of genetic modification in agriculture and the available as well as the required structures for promotion of transgenic technologies in the region.

The Driving Forces

The evolution of population and its rate of growth in Africa provides the basis for the widespread economic crises the continent is now witnessing. Africa has a population of about 520 million people and this is projected to increase to 1.3 billion in the next 25 years. More than 80% of this population as well as over 30% of their Gross Domestic Product depend on agriculture. Any factor therefore, which destabilizes the performance of agriculture produces direct and severe consequences to the well-being of the people. Africa unlike any other region in the world has the lowest average crop production per unit area of farmed land. For example, the average maize yield in the USA in 1997/98 was 8.1 tones per hectare providing a total annual production of 263 million tones of maize in the country from 32 million hectares of land. During the same period the whole of sub-Saharan Africa planted 22 million hectares of maize with an average yield of 1.2 tones per hectare. The total annual production in 44 countries in the region was 26 million tones of maize (Chetsanga, 1999).

The production of sweetpotato, a staple crop in the region is 6 tones per hectare compared to the world average of 14 tones per hectare. China produces, three times the average in Africa (Wambugu, 1999). These low yields per hectare frequently result in severe food deficits which often leads to mass starvation or large food imports. Africa imports at least 25 percent of its grain requirement (Wambugu, 1999).

The major underlying factor in the low crops production is frequent rainfall failures which directly translate into severe droughts and massive crop failures. This problem is often exacerbated by the occurrence of vast areas of unfertile soils that cannot support crop production. In addition, numerous plant diseases and pests are found in Africa.

Large proportions of the African communities inhabit the vast marginal lands and millions live in urban centres. Because of their environments, people cannot produce adequate food to meet their nutritional and other socio-economic requirements. The majority of the people thus live in abject poverty (Ndiritu, 1999). More than 200 million people i.e. over one third of Africa's population suffer chronic undernutrition, subsisting on less than 2100 kilocalories per day. This is the lowest level of per capita food availability of any region in the world. To combat these crises, Africa more than any other region urgently needs technologies which enable agriculture to reduce losses, increase yields and minimize environmental impact.

Status of Transgenic Technologies in Africa

Globally, biotechnology and molecular biology in plant breeding is already offering unprecedented range of choices for making the future of agriculture more productive and sustainable. The need for biotechnology in Africa is considered in the context of the continent's need for more food for its people. Biotechnology - derived solutions for the agricultural problems indicated above if built into the genotypes of plants could reduce the need for water as well as the deleterious effects of diseases and pests thus promoting sustainable agriculture in Africa.

To address the issue of soil fertility and the requirement for expensive fertilizers, a number of countries have embarked on the use of Rhizobium inoculation of plants. The application of tissue culture is employed to address constraints of availability of adequate disease free planting materials and rapid improvement in crop production.

There has been very little application of genetic modification of plants. This has mainly been due to Africa's many problems including shortage of skilled people and lack of enabling policies. The recently emerged public concern regarding the use of genetic modification of crops has further stifled Africa's efforts in genetic enhancement.

In spite of this, genetic engineering to produce transgenic crops is considered highly relevant to Africa in as far as addressing agricultural production constraints such as high chemical inputs, yield losses arising from pest and disease damages and drought tolerant crops is concerned. Based on this conviction, a number of countries in the region have made decisions and commitments and have taken steps to invest in genetic modification in agriculture, particularly in the areas of major staple foods and commercial crops like maize, potato, sweetpotato, tomato, beans, sugarcane, cotton and tobacco. These countries include Egypt, South Africa, Kenya, Zimbabwe and Mauritius.

In Egypt, the Agricultural Genetic Engineering Research Institute (AGRERI) established in 1990 has adopted genetic engineering to address major problems of agriculture in the country. The specific projects at AGERI on transgenic crops are shown in table 1 and include development of virus, insect and fungal resistant crops as well as stress tolerance and protein engineering.

Table 1: Current projects at AGERI on transgenic crops

	Potato	**Tomato**	**Cotton**	**Maize**	**Faba Beans**	**Cucurbits**
Virus resistance	✓	✓			✓	✓
Insect resistance	✓	✓	✓	✓		
Stress Tolerance		✓	✓		✓	
Genome mapping		✓		✓		
Protein engineering					✓	
Fungal resistance		✓	✓	✓		

Source: Magdy Madkour, 1995

The Republic of South Africa is perhaps the most advanced nation in Africa in the development and enhancement of agriculture through genetic modification of crops. Numerous biotechnology centres comprising national agricultural research organizations, universities and commercial companies are engaged in a wide range of transgenic crops development in partnership with international companies and programs. As shown in table 2, these organizations and companies are engaged in transgenic crops development for fungal, viral, insect and drought resistance ranging from food crops such as potatoes, tomatoes and maize to industrial crops and forest trees such as cotton, tobacco, sugarcane, sunflower, pines and eucalyptus.

Table 2: Selected South African companies involved in biotechnology projects or products with international partners

SA Co./Org	Product
CSIR	Herbicide resistant soybeans, maize, tomatoes Pine and eucalyptus
ARC	Virus resistant ornamentals, curcubits, potatoes Fungal resistant cotton, tobacco
AgrEvo	Herbicide resistant maize and soybeans
National Chemical Products (NCP)	Biocontrol and biofertilizer
Monsanto	Bovine somatotropin
Hedeco	Micropropagation of disease free ornamental bulbs
PHI Genetics	Maize, soybeans, sunflower and sorghum
Sensako	Virus resistance in maize Pest resistance in wheat Molecular markers in breeding program
Pannar	Modification in sunflowers
Carnia	Canola and maize
Carnia	Soybeans
Mayfords	Genetically improved tomatoes
Clark cotton	Bt transgenic cotton

Source: Jocelyn Webster and Muffy Koch, 1995

Countries such as Kenya, Zimbabwe and Mauritius have also initiated development and evaluation of transgenic crops.

In Kenya, the Kenya Agricultural Research Institute (KARI) was established in 1986 as the main agricultural research organization in the country. Since 1991 the Institute has been involved in the development of transgenic sweetpotato resistant to Feathery Mottle Virus (Wafula, 1993) and has plans to initiate development of Bt transgenic maize against stem borers (table 3).

Zimbabwe and Mauritius have on going transgenic crops development projects in sugarcane focusing on virus - and - pest resistant products (Wambugu, 1999). In addition Zimbabwe has for sometime been conducting a field evaluation of trangenic Bt cotton. Other countries in the continent are either at the stage of identifying national priorities for biotechnology or are in the early stags of establishing the requisite capacities in genetic engineering and molecular biology.

Table 3: Transgenic crops projects in the rest of Africa

Country	Transgenic crop projects
Kenya	Virus resistant sweetpotato Bt maize (Planned)
Zimbabwe	Bt cotton Virus and insect resistant sugarcane
Mauritius	Virus and insect resistant sugarcane

In spite of the above developments, the survey on commercialized global transgenic crops shows that Africa has less than 1% of the global hectares under transgenic crops as compared to 72% in the USA (James, 1999).

Future Direction

The African continent, given its numerous and unique problems perhaps needs biotechnology including transgenic crops more urgently than ever before to improve its food production levels. The continent cannot afford to stay on the sideline of the current technological revolution. Contrary to the raging debate that genetic modification in agriculture bears no potential benefit for Africa but only disaster emanating from food toxicity and allergenicity, gene flow and transfer to other species, incapacity to capture commercial and production benefits and erosion of biodiversity, the continent stands to benefit enormously in terms of food production levels and environmental conservation. While history shows that new technologies are not without risk, it also teaches us that benefits of a new technology can be much greater than the risks. Hence the assessment of risks in the light of benefits ought to be the essence of making choices for genetic modification in agriculture.
What Africa needs is first to establish confidence in, and view biotechnology as a critical enabling technology that is very broad and which offers many platforms for building a sustainable future Africa.

Second, Africa will need to listen and adjust its position on important issues that will guide its development, testing and application of new products based on biotechnology. It will need to develop capacities and establish public instruments to carry forward or audit additional research necessary to ascertain freedom of products of biotechnology from the elements of public concern.

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Issues and Perspectives of Transgenic Crops in the Asia-Pacific Region

During 1998, nearly 12 million hectares were under transgenic crops with most of the area covered by genetically modified (GMO) soybean, maize, cotton and canola (mustard). Nearly 75 percent of the area under GMOs was in the United States of America, where the regulatory measures in force seem to ensure that the public have confidence in the environmental and nutritional safety of GMOs. This is not the case in India as well as in European Union countries.

Agricultural strategy for the 21st century, in countries like India and others in the Asia Pacific region, will have to place emphasis on producing more per units of land, water, energy, time, capital and labour, though pathways that will ensure that the productivity improvement is not associated with long term ecological and/ or social harm. Also agriculture has to be a key instrument for producing not only more food but also more income and jobs. It is in this context that the new opportunities opened up by genomics and molecular breeding for fostering sustainable advances in crop and farm animal productivity and quality will have to be assessed carefully for their benefits and risks.

Research carried out with the new genetic technologies during the last 15 years has shown that they can help to improve crops in more precise and faster ways as compared to the traditional Mendelian methods. Designer crops based on novel genetic combinations created by moving genes across sexual barriers are now becoming available. Opportunities for breeding varieties for resistance/ tolerance to biotic and abiotic stresses and drought and salinity tolerance and as well as for improved nutritional qualities are particularly important for farming families struggling to improve yields and quality under unfavourable growing conditions. It is such opportunities that are leading to increasing investment in agricultural biotechnology by both the public and private sectors in India. While industrial countries are making greater investments in medical biotechnology as a result of their priority for better health security, India's emphasis has been more on agricultural biotechnology because of the need to ensure food and nutrition security for current and future populations.

While the benefits are attractive, Recombinant DNA technologies resulting in genetically modified organisms (GMO's) have also aroused widespread public concern in several respects some of which are the following :

- Direct effects of the transferred genes on the recipient organism(s)
- New possibilities for unfavourable recombinations
- Behaviour of the GMOs in field situations
- Effects on environment and biodiversity
- Nutritive properties of the food produced by GMO's

In addition, the impact of new technologies such as “gene protection technology” and the growing expansion of proprietary science on small and resource poor farming families who save seeds to raise crops, needs careful consideration and monitoring.

The existing regulatory mechanisms for the GMOs in these countries however seem to be inadequate for instilling the requisite degree of public and media confidence in relation to bioethics and biosafety. Therefore, no further time should be lost in introducing an integrated *precautionary package* which will help the country to derive benefits from genomics and molecular breeding of crops and farm animals without associated environmental, social and health risks.

The M. S. Swaminathan Research Foundation, Chennai is in the forefront for ensuring effective use of sefe and sustainbale technologies in the region through multi-stakeholder discussions, consultations, debates and deliberation. The Foundation firmly believe thet following steps are essential for intensifying the use of *Biotechnology for the Public Good.*

- Promoting greater interaction between public and private sector scientists, civil society organisations, the media and the judiciary and organisation of interactive workshops for this purpose.
- Information empowerment and education at all levels, starting with the village panchayats.
- Integration of GMOs within an integrated natural resources conservation and enhancement strategy, such as including GMOs in the context of an IPM framework in the case of pest management.
- Increasing the national capacity in assessing known and unforeseen risks and in developing an unbiased balance sheet of risks and benefits.
- Intensification of research in the public sector and expanding meaningful public-private sector partnerships.
- Strengthening the infrastructure for research on microorganisms as well as farm animals, including fish.
- Introducing special demonstration, training, credit and extension programmes to take the benefits of transgenics to the economically under-privileged farming families.
- Developing coordinating and educational mechanisms at the national, state and panchayat levels which will inspire public confidence and public acceptance of GMOs.
- Promoting a Knowledge System for Sustainable Food Security based on the integration of traditional and new technologies.
- Fostering greater international cooperation based on national priorities and interests.

The Asia-Pacific region is rich in Biodiversity, which serves as the primary feedstock for biotechnology. Several mega-biodiversity areas occur in this region. The centres of origin and diversity of crops like rice, sugarcane, coconut, jute and cotton occur in countries of Asia and the Pacific. The region accounts for more than half of the world's population and a considerable proportion of the world's poor. Thanks to advances in science and technology supported by appropriate public policies, the farm families of this region have been able to keep food production above the level of population growth during the last 25 years. However, the challenges ahead are greater and there is growing concern about the future of food security in this region.

Some of the Asian countries such as China, India, Japan and Thailand are already engaged in the field testing and release of transgenic crops, while others are in different stages of finalising the field testing aspects of their biosafety regulations. Most of the regulations in these countries pertain to the release of agrochemicals, biological control agents and new plant varieties and therefore are relevant to the products of modern biotechnology as well as more conventionally produced products. These regulations provide necessary protection to ensure that the products of biotechnology will not be marketed without prior approval. Globalization of trade and commercialization of the genetically modified products, therefore, requires countries to develop science-based risk assessment systems comprising of active and well informed national review bodies. The national review bodies in individual countries should be kept informed of the assessments and current policies of functioning national biosafety review committees in other countries, particularly in connection with environmental risk assessment procedures. Biosafety reviews following national guidelines should be conducted prior to release of genetically engineered organisms.

In most of the countries in this region lack of sound regulatory review process could be attributed to the lack of sufficient expertise in the field of biotechnology research itself. For such countries considering possibility of adopting new technologies, it is important that precise national need be determined from the wide array of products, processes and areas of reassert that biotechnology offers. Introducing a capacity in biotechnology is difficult, particularly for countries with a weak base in agricultural sciences, as in case of most of the countries in the Asian region. Adoption of modern biotechnology will in no way deminish the need for conventional agricultural research in these countries. Rather, the demand for new expertise and companion facilities will exert additional pressure on the already limited resources. Close attention therefore will have to be given to the pattern of assistance to agricultural research, with changes introduced to encourage equity funding between private industry and public sector organisations.

Factors that favour the entry of developing countries into biotechnology are their large and growing domestic markets, the opportunities to identify niche markets in which the major transnational companies are neither active nor interested and the existence within these countries of plant genetic resources for many of the world major agricultural crops. Capacity building in both biotechnology research and regulatory mechanisms therefore holds the key for adoption of new genetic manipulation technologies for ensuring food security in the countries of Asia.

Technical barriers in these countries for the promotion of biotechnology include lack of clear-cut regulatory authority that has the capability to conduct scientific and technical reviews to determine the potential environmental impact issues of genetically engineered organisms, and also the related biosafety issues. This is the first critical step to facilitate commercialisation of genetically engineered crop plants. This necessitates the strong need for developing scientific capability and critical and credible manpower to study the biotic effects of biotechnology research and field tests of transgenic crops. It is essential to develop a pool of qualified scientific and regulatory personnel to review and document biosafety and environmental impact assessment of transgenic plants so that they can confidently satisfy the environmental activists and critics who are concerned about biosafety. Effective regulatory responsibilities and networking capabilities in the region should be the first step in promoting the biotechnology rerearch and ensuring that issues of public good are addressed in future.