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Why there is no Transgenic Papaya in Mexico

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ABSTRACT

Mexico is the world's second largest papaya producer and its top exporter. *Papaya ringspot virus* (PRSV) may cause commercial crop losses of up to 100% in some regions, especially affecting small, low-income, and medium sized papaya producers. The introduction of genetically engineered (GE) PRSV-resistant papaya could therefore help alleviate this problem. Scientific expertise for in-country development of GE PRSV-resistant papaya is already in place and the regulatory, intellectual property rights and public perception settings are encouraging. The introduction of GE papaya would be greatly facilitated by the fact that a single variety, 'Maradol', would need to be modified for adoption since it completely dominates local and export markets. However, part of Mexico is within the proposed center of origin of *Carica papaya*. Risk assessment of GE PRSV-resistant papaya should consider transgene flow to cultivated, wild or weedy relatives. The role of farmers' practices and social values as well as the structure of the papaya seed system in shaping the nature of gene flow needs to be investigated. What then has hampered, over the last 20 years, any serious efforts to develop, introduce and evaluate this technology? An *ex ante* assessment of the socioeconomic impact of GE papaya is being conducted to foresee possible impacts of transgenic papaya, taking into consideration the prevailing agricultural production systems. Current data indicate that resource poor farmers would benefit most from this technology but that large producers are averse to its introduction. Moreover, two foundations whose main objective is to facilitate the development and transfer of innovative technologies to farmers, have dropped their support of two public projects for the development of GE papaya.

Keywords: biosafety, genetic diversity, public perception, ringspot virus, socioeconomic issues

Abbreviations: amiRNA, artificial microRNA; ***bar***, Bialaphos resistance gene; **Bt**, *Bacillus thuringiensis*; **CIBIOGEM**, Inter-Secretarial Commission on Biosafety of Genetically Modified Organisms; **Cinvestav**, Centro de Investigación y Estudios Avanzados; **CP**, Coat protein; **DGSV**, General Directorate of Plant Health of the Ministry of Agriculture; **EACR**, European Association for Cancer Research; **EPA**, Environmental Protection Agency; **EU**, European Union; **FAO**, Food and Agriculture Organization of the United Nations; **GE**, genetically engineered; **HA 5-1**, attenuated Hawaiian viral strain 5-1; **hpt**, hygromicin phosphotransferase gene; **siRNA**, small interfering RNA; **INIFAP**, National Research Institute of Forestry, Agriculture and Livestock; **IPR**, Intelectual Property Rights; ***npt*II**, Neomycin phosphotransferase gene giving resistance to kanamycin; **PapMV**, *Papaya mosaic virus*; **PRSV**, *Papaya ringspot virus*; **PTGS**, post-transcriptional gene silencing; **SAGARPA**, Ministry of Agriculture, Livestock, Rural Development, Fisheries and Food; ***uidA***, β-glucuronidase gene; **WHO**, World Health Organization

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INTRODUCTION

The first application for the deregulation of a genetically engineered (GE) crop in Mexico was submitted in 1988 (Sarukán 1999). This prompted the formation, in 1991, of the National Agricultural Biosafety Committee, under the umbrella of the Plant Health Office of the Ministry of Agriculture (DGSV-SAGARPA). Seventeen years later, after many applications and contained field experiments of transgenic cotton, soybeans, maize and other minor crops, large scale experimental field trials of GE cotton, a politically motivated *de facto* moratorium on all transgenic maize trials in 1998, and endless controversies, congress voted the Biosafety Law for Genetically Modified Organisms (DOF

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2005). However, it was not until early 2008 that the regulations for the application of this law were eventually approved and released (DOF 2008).

As in many other nations, there are polarized views on GM organisms and the potential of biotechnology for solving food problems.

It is against this backdrop that we will consider the question of why there is no transgenic papaya in Mexico. We shall endeavor to show that the scientific expertise for in-country development of GE papaya is already in place, and that the regulatory, intellectual property rights and public perception settings are encouraging. However, potentially major hurdles can be anticipated in relation to the resolution of risk assessment issues and the current perception that barriers to transferring the technology to papaya producers may be in the producers themselves, at least for a few years to come.

THE PAPAYA IN MEXICO

A glimpse of production figures

Worldwide papaya production and trade have changed dramatically over the last 30 years. While world production has increased from about 2.5 to 7.1 M tonnes (t) (data for the period 1980-2006), there has been a jump of more than 12-fold in worldwide exports and of 22-fold in imports (FAO 2009b), at roughly 0.25 Mt in each case. Mexican production has increased from about 200,000 to 800,000 t in the same period; as the second world producer, its output is less than half that of Brazil. Mexico's exports have gone from almost none in 1980 to 95,000 t in 2006 to become the world's top papaya exporter, a record that almost doubled that of its closest competitor (Malaysia) and represented around 35% of the global papaya trade market in 2006. The bulk of Mexican exports are to the USA, a country where imports have increased from roughly 15,000 to 132,000 t in three decades. Albeit these trends have declined sharply in the last decade, it is clear that papaya consumption has rapidly gained acceptance, especially in industrialized countries where there has been a more general increase in the consumption of fruits and vegetables (FAO 2009a, 2009c).

In Mexico, 20 of the 32 states are papaya producers (SIAP 2009b). In the past few years, Veracruz, Chiapas, Oaxaca, Colima, Michoacán, Yucatán, Tabasco and Guerrero have been the eight states with the largest planted area, contributing to 88% of national production. Yield within these states varies from 24 to 80 t/ha with an average 45 t/ha. The national average yield was 41 t/ha, and the total planted area was 19,500 ha (SIAP 2009a). By comparison, the average yield in Thailand was 12 t/ha, in Brazil 51 t/ha and in El Salvador 133 t/ha (FAO 2009b).

Before the 1970's, 'Amarilla' and 'Amameyada' were the main papaya varieties cultivated in the country. However, Mexico owes much of its success as a producer and more particularly as exporter to the adoption in the 1970s, and spectacular expansion in the 1980s, of the Cuban 'Maradol' variety. Production under irrigation covered about half of the total planted area in the country in 2006; the average yield under these conditions was 55 t/ha. Under rainfed conditions, the average yield was 28 t/ha (SIAP 2009a). The average price of the harvest is highly variable under rainfed conditions and is always lower than under irrigation, a reflection of concomitant differences in fruit quality under the two systems. Pre-harvest diseases, generally more common and severe under rainfed conditions, are the main cause of yield reduction and fruit damage.

Production systems – socioeconomic considerations

In order to foresee the possible impact of transgenic papaya in Mexico, an *ex ante* socioeconomic study is being conducted, focusing on the states of Veracruz, Chiapas and Colima. The first two are the most prominent producers while Colima is home to the first producer-driven research project on the development of transgenic papaya (Castañeda *et al.* 2007; Castañeda 2009). The overall objective of the *ex ante* study was to *forecast* the socioeconomic impacts of a new technology, namely PRSV-resistant GE papaya, prior to its introduction. Specific objectives centered on identifying salient potential economic impacts on producers and seed companies in terms of production costs, market competitiveness, seed distribution, etc., with a view to pinpoint factors that would help improve the impoverished situation of small, low income, producers.

The study comprised three stages. Initially, the authors held interviews with carefully selected "key informants" representing producers, agricultural researchers, government officials and members of pertinent local institutions, in five of the seven most important papaya producing regions in Mexico. Thus, the state of Veracruz was chosen for conducting a survey that would target low income farmers. In the second phase, a focus group (Elliot *et al.* 2005) involving a small group of stakeholders, was set up to help design the survey questionnaire on the basis of farm survey and cost-benefit analyses. In the third phase, fifty eight small papaya producers from the small county of Cotaxtla provided answers to 105 questions designed to probe agricultural practices, socio-economic variables and values and perceptions concerning new technologies and GE papaya in particular.

Here we briefly summarize salient findings on the basis of a simple definition of production systems in terms of three broad groups of farmers/producers: very low income farm households that depend on small-scale subsistence production, medium-sized farms, and large-scale producers. These characterize Mexican agriculture and serve as a starting criterion to assess social impacts of new technologies (Brush and Chauvet 2004; Nivia and Perfecto 2009).

Low income, small-scale producers have orchards that range from 0.5 ha to 5-10 ha, mostly on rainfed land, with yields ranging from 35 to 50 t/ha. Similar areas are dedicated by farmers to producing other crops such as maize (Soleri *et al.* 2005), or various organic products (Tovar *et al.* 2005). This papaya production system is found in Veracruz, Chiapas, Michoacán, Jalisco, Oaxaca and Yucatán. Its produce is generally limited to the domestic, often local, market. Marketing involves intermediaries who buy the product directly from the farmers and place them at a disadvantage by unilaterally establishing the sale price. Moreover, if there is a large supply of papaya on the market, the price paid by the broker does not cover production costs and producers prefer to lose their harvest. Having limited access to information, technology and financing opportunities, these producers are likely to suffer most from any contingencies affecting the health of their crop. They may receive some technical assistance from distributors of agricultural inputs but will be very much on their own if their crop fails (Castañeda 2009).

Medium scale farms, usually 20 to 30 ha in size, generate enough income to attract private loans at very high interest and therefore remain financially vulnerable. Marketing and crop risks are similar to those of small scale producers. However, in good years, they will seek professional assistance and will implement more intensive crop management practices such as drop irrigation.

Large-scale producers normally plant an area of 100 to 150 ha under irrigation.

Reported yields range from 140 to 200 t/ha. They contribute to both domestic and international markets, with most exports going to the United States of America. Their investments are large and risky, and include expenditures in local and foreign specialized technical assistance; the main yearly risk is the loss of the crop during the hurricane season in coastal regions. In some regions, labor shortages due to migration cause steep wage increases in order to retain migrant workers, a practice that only large producers can afford (Massieu 2009).

Seed supply

Seed supply is another pertinent aspect of the production systems described. There are three seed supply channels: the seed that mostly low income producers select from their own orchards and backyards; the seed obtained from the National Research Institute of Forestry, Agriculture and Livestock (INIFAP); and the seed purchased from mostly one commercial source (Castañeda *et al.* 2007).

The "Sistema Producto" - a national program designed to strengthen agriculture supply chain linkages and improve access to market opportunities for small-scale producers has not yet been properly integrated into the papaya seed production process. This program could eventually play a role in a timely and successful adoption of new varieties and technologies by small producers.

Major diseases and genetically engineered (GE) papaya – PRSV as a case in point

In Mexico, the papaya crop is affected by diseases caused by bacteria (e.g., *Erwinia* and *Pseudomonas* spp.), fungi (e.g., *Cercospora* and *Fusarium* spp.), phytoplasmas, nematodes and viruses. Papaya ringspot, caused by the potyvirus *Papaya ringspot virus* (PRSV), is arguably the most devastating disease in Mexico and worldwide (Poghosyan *et al.* 2007). Although the pressure of PRSV remains high throughout the year, in regions of high rainfall such as Chiapas, fungi represent a greater threat to plant health.

The development of GE PRSV-resistant papaya essentially saved the Hawaiian papaya industry (Gonsalves 1998; Stokstad 2008). It is unquestionable that resistance to PRSV, introduced by either conventional methods or genetic engineering, would benefit Mexican producers in at least two ways. First, it would reduce production costs and increase yields. Second, it would help reduce one of the main problems affecting harvested fruit quality, namely the unsightly tainting of fruits with PRSV ringspots (generally, this does not affect pulp quality) which in turn make the fruit more vulnerable to opportunistic fungal attack and thus a reduction of shelf life.

Experimental attempts to control the deleterious effect of PRSV using cross protection were carried out using the PRSV attenuated strain from Hawaii (HA 5-1) without success. Indeed, efforts to obtain Mexican attenuated strains could not be completed since the Mexican PRSV isolate from Veracruz did not produce local lesions in the experimental host *Chenopodium quinoa* (Téliz *et al.* 1991) and the strategy came to a halt. A search for a natural mild PRSV strain, to confer cross protection is underway (unpublished results).

In 1997, a major producer from the state of Chiapas submitted an application to the Mexican Biosafety authorities for field testing of a GE 'Sunrise' variety developed and transferred by D. Gonsalves (SENASICA 2003); this variety harbored an untranslatable CP sequence of HA5-1, the Hawaiian PRSV isolate (Gonsalves *et al.* 1998). A small plot of less than a tenth of a hectare was set up but was later swept away by hurricane Pauline and the project was abandoned. Four more applications for small greenhouse and field trials of GE papayas for long shelf life and PRSV resistance were submitted in 1998-9 by a multinational company (SENASICA 2003); these applications were approved by the DGSV (SAGARPA) but, for unknown reasons, all the experiments were cancelled by the applicants at the end of 1999. No more applications for transgenic papaya have been submitted since then.

PAPAYA RINGSPOT VIRUS (PRSV) – PREVALENCE AND DIVERSITY IN MEXICO

Prior to the spectacular expansion of the area planted to 'Maradol' papaya, PRSV was a minor threat with little or no effects on labor costs. PRSV was reported for the first time in México in 1974 (Ochoa de F. and Galindo 1977) with commercial losses of up to 100% especially affecting small, low-income, and medium sized papaya producers (unpublished data). Its presence was detected in all three commercial papaya producing States at that time: Veracruz on the East coast, Colima on the West coast and Guerrero in the Southwest. This preceded the introduction of 'Maradol' as the most widely grown variety in Mexico (SAGARPA 2005). At present, all twenty states where papaya is grown commercially are affected by PRSV. The virus causes damage that ranges from mild, mostly in areas with major producers, to very severe in areas belonging to medium or small scale producers (Noa-Carrazana *et al.* 2006). The reasons behind these important differences between production systems, reasons that impinge directly on the potential adoption of transgenic PRSV resistant papaya, were discussed in the previous section.

Another issue that will affect the development and acceptability of resistant transgenic papaya in Mexico is the high variability of the virus across the country. Indeed, it has been shown that the CP mediated protection of transgenic lines (as well as classical cross protection), does not always provide broad protection against geographically diverse PRSV isolates (Tennant *et al.* 1994; Gonsalves 1998; Chiang *et al.* 2001; Tennant *et al.* 2001; Bau *et al.* 2003). Two reports have been published about the distribution and variability of PRSV isolates in Mexico (Silva-Rosales *et al.* 2000; Noa-Carrazana *et al.* 2006). Infected plants were collected in all papaya production areas in Mexico from 1995 to 2002. PRSV was present everywhere and was isolated from different papaya cultivars grown in the country (i.e., 'Amarilla', 'Cera', 'Amameyada' and 'Maradol'). The virus was also present in some feral cucurbitaceous species and in wild papaya (possibly *Jacaratia*) species in the vicinity of sampled plantations. This is suggestive of the presence of PRSV before the large scale production of the fruit started in this country. The study of the diversity of PRSV was carried out by analyzing the nucleotide sequence of the CP gene; in contrast to PRSV isolates from other world locations (Bateson *et al.* 1994), there was a correlation between geographical origin and isolate variation in Mexico (Noa-Carrazana *et al.* 2006). At least six putative viral variants have been detected on the basis of CP gene variation, classified according to their geographic origins: 1. Chiapas, 2. Oaxaca, 3. Michoacán, 4. Jalisco-Nayarit, 5. Veracruz-Tabasco and 6. Veracuz-Yucatán. Each corresponds to a distinct physiographic region separated by topographic barriers from other regions and characterized by a combination of climatic conditions and vegetation types (Noa-Carrazana *et al.* 2006).

Thus, transgenic papaya with broad resistance to diverse PRSV isolates prevalent in Mexico can be developed by stacking the current battery of viral genes isolated by scientists from Cinvestav-Unidad Irapuato where the research was carried out.

DEVELOPMENT OF TRANSGENIC PAPAYA IN MEXICO

Molecular biology tools to engineer different plants of economic importance had their impact in Mexico, as in many other countries, in the mid eighties. At that time, there were only a couple of research institutes in Mexico that spread the knowledge and technical skills to other institutions across the country. By 1995, papaya embryogenic callus had been genetically transformed using *Agrobacterium tumefaciens* and microprojectile bombardment; three novel traits were introduced into papaya plants: the first, mostly a proof of concept, was herbicide resistance (Cabrera-Ponce *et al.* 1995); the second was the overexpression in roots of citrate synthase from the bacterium *Pseudomonas aeruginosa*, as a means to develop a model system for the study of aluminum tolerance (de la Fuente *et al.* 1997); and the third was resistance to PRSV using the *CP* gene from a severe viral Mexican isolate from Veracruz (unpublished data). These studies were conducted at Cinvestav-Unidad Irapuato, in Mexico. The PRSV resistant plants were obtained in 1997 as part of a project funded by the 'Fundación Produce Tabasco', one of 32 state foundations whose main objective is to facilitate the development and transfer of innovative technologies from public and private research institutions to more than 3500 registered producers (COFUPRO 2009). However, by 1999, as a result of a reorganization of the foundation, interest in transgenic papaya died out and the project was dropped. More recently, a sister foundation from the state of Colima – 'Fundación Produce Colima', acting on behalf of local papaya producers, funded a two year pilot project for the development of transgenic 'Maradol' papaya, run by INIFAP, whose main outcome was the establishment of standard protocols for routine transformation (Guzmán-González *et al.* 2006); but the project was not allowed to continue into its second phase when the local producers changed their priorities in the face of funding reductions. At present, an ongoing collaboration between the University of Colima and Cinvestav-Unidad Irapuato is developing a strategy to stack multiple *CP* genes belonging to different strains isolated during the PRSV diversity study at the latter institution (Noa-Carrazana *et al.* 2006). Marker-free technologies (Darbani *et al.* 2007) and other innovations in transformation methodologies, such as targeted homologous recombination (Hanin and Paszkowski 2003), the use of untranslatable RNA-mediated virus resistance (Bucher *et al.* 2006; Prins *et al.* 2008) and strategies using amiRNA (Niu *et al.* 2006; Qu *et al.* 2007) or chimeric hairpin RNA to produce siRNA (Yan *et al.* 2010), are being investigated in order to simplify risk assessment and increase the likelihood of deregulation and adoption. Untranslatable virus-derived transgenes are particularly interesting since little or no transgene mRNA accumulates as a result of post-transcriptional gene silencing (PTGS), especially in plants expressing the highest resistance levels (Lindbo *et al.* 1993). Therefore, apart from the triggering of PTGS as a defense mechanism, there are no traces left of viral transgene products. It remains to be seen whether there are any risks associated with the consumption of plant products in which the PTGS system is always turned on.

In essence, the know-how, the pertinent gene constructs and scientific collaborations are already in place for the successful development of second generation GE PRSV-resistant papaya in Mexico. However, neither the producers nor the government facilitators of technology transfer have shown sustained interest in the adoption of this proven technology.

MEXICAN BIOSAFETY

At the end of 1999, an Inter-Secretarial Commission on Biosafety of Genetically Modified Organisms (CIBIOGEM 1999a) was established in Mexico with the participation of six ministries (Treasure, Environment, Health, Agriculture, Education and Commerce), plus the National Council for Science and Technology. Its mandate is to coordinate the policies and federal regulation of activities related to Genetically Modified Organisms (GMOs), including production, imports, exports, mobilization, transportation, cultivation, consumption, and general use of GMOs and their products (DOF 2005). The first Law on Biosafety of Genetically Modified Organisms was approved in Mexico in 2005 (DOF 2005). It encompasses all aspects related to the use of transgenics in agriculture. A biosafety regulation, emanated from the law, was published in 2008 (DOF 2008) and amended in March 2009 to treat maize as a special case, thus lifting the politically motivated moratorium that had been imposed *de facto* eleven years earlier (DOF 2008). Under the Biosafety Law, promotion of national research that benefits and helps to solve national problems of agro-forestry producers is envisaged.

Twenty one years after the submission of the first application for growing transgenic tomatoes, Mexico is witness to the beginning of a new era of opportunities for the development of GE crops. Notwithstanding this new scenario, there are many obstacles to overcome as exemplified by the thorough documentation on the deregulation of GE papaya in Hawaii (Susuki *et al.* 2008). The coordinated, risk-based system implemented in the USA, was set up to ensure that new biotechnology products are safe for the environment and human health. In the case of GE papaya, it took a record eight years from the time of creation of GE PRSV-resistant R0 line 55-1 hemizygous for the *CP* transgene, to the obtaining of the license agreements that allowed the commercial cultivation of transgenic papaya and its derivatives in Hawaii only, and the first release of seed to farmers (Susuki *et al.* 2008), followed by a remarkably rapid adoption (Gonsalves *et al.* 2007).

Risk assessment and management issues

In the case of transgenic papaya in Mexico we foresee at least two technical stumbling blocks related to satisfactorily clarifying potential risks of (i) virus recombination and, (ii) transgene flow to wild or weedy relatives and to non-GE papaya ("coexistence"). Of these, the former has been addressed and reviewed for various plant-virus systems without convincing evidence of an environmentally deleterious effect (Prins *et al.* 2008); however, each case should be monitored in its own right. Coexistence, on the other hand, is probably a more difficult issue. Indeed, Southeastern Mexico is considered to be within the broad area believed to be the center of origin of papaya and its domesticates (Badillo 1971). Although conspecific wild and weedy *Carica papaya* plants have not been collected in any systematic way in Mexico, their existence in Veracruz and South to Chiapas and the Yucatan is sparsely documented with detailed botanical descriptions based on herbarium specimens in Mexico and elsewhere (Moreno 1980; Paz and Vázquez-Yanes 1998). Little, if anything, is known about gene flow between domesticated papayas and their conspecific wild relatives. However, the potential for intraspecific and intravarietal gene introgression is undeniable. Pollination strategies in *Carica* involve hawk moths (Sphingidae), (Martins 2004) powerful flyers that can transport pollen between distant plantations (Morrisen 1995). Natural hybridization with its closest wild species relatives, namely *Vasconcellea* spp., is hampered by strong hybrid infertility, indicating that gene transfer between *C. papaya* and other species in the wild is expected to be negligible (Van Droogenbroeck *et al.* 2004). If transgenic papaya were to coexist with non-transgenic papaya in close proximity, a significant concern would arise, especially in the case of small producers who might not want to adopt GE papaya and are growing indigenous and naturalized varieties or organic papaya (Lotter 2005; Manshardt *et al.* 2007).

The experience acquired with the presence of transgenic maize in Mexico (Raven 2005) and the dispersal of transgenes through maize seeds (Dyer *et al.* 2009) should further help design risk assessment strategies for transgenic papaya in Mexico that take farmers' practices into account (Bellon 2004). In traditional maize farming, multiple maize populations coexist and most seed is saved from the previous harvest; moreover, farmers may mix seed from various sources either to help ends meet or to expressly introduce new variation (Perales-Rivera *et al.* 2003). Practices like these inevitably increase gene flow at various stages of the cropping cycles. Recent hard data on the presence of transgenes in maize across Mexico, has shown quite forcefully that farmer's practices as reflected by seed systems and grain markets are key to understanding transgene dispersal and survival (Dyer *et al.* 2009).

The risk management process during potential or actual GE crop adoption, should also include social and cultural issues that take into consideration the agricultural knowledge and the values of as many pertinent stakeholders as possible, especially those that may benefit most from the technology such as small-scale producers (Soleri *et al.* 2005). Moreover, recent research based on extensive interviews has indicated that resource-poor maize farmers in

Cuba, Guatemala and Mexico, contrary to established wisdom, preferred to avoid GE maize varieties for sowing and eating thus appearing to be "risk averse" (Soleri *et al.* 2008). The authors also argued that their data demonstrated that GE maize is not an optimal solution in many cases and that alternative technologies have not been evaluated properly.

The case of GE papaya is, at least in principle, rather different: small farmers aiming at selling their crops at higher prices cultivate 'Maradol' and derivatives in order to compete with larger producers. Thus, in contrast with maize, this very narrow genetic base should facilitate the introduction of PRSV resistant types developed by conventional methods or genetic engineering. Their main concern regarding GE papaya is the perception that they would need to pay a "high" price for GE papaya seed that would be bought from the private sector (Castañeda *et al.* 2007). This is not necessarily so as has been clearly shown by the Hawaiian experience: first, the technology was developed and deployed by academics (Gonsalves *et al.* 2007); second, GE seed was distributed free of charge along with an educational and promotional campaign in order to jumpstart adoption quite successfully.

Large producers, who could afford the adoption of new technologies such as PRSV resistant GE papaya and thus reap its benefits, have learned to "live with the virus" (Castañeda *et al.* 2007). The increased impact of PRSV with the adoption of 'Maradol' papaya has led these producers to change their crop management practices, including intensive weeding, constant crop surveillance and destruction of diseased plants, insecticide applications to keep the aphid vector populations in check, and so on. They will even buy out and destroy neighboring diseased plantations in order to lower the risk of spread of the pathogen to their crops. In their opinion, the presence of the virus represents an entry barrier for competitors as not all farmers are able to keep a careful management plan. Having virus-resistant GE seed would decrease production costs and encourage new investors into the papaya agribusiness.

Other issues, such as the safety of the product and its derivatives for human consumption, will certainly benefit from the Hawaiian experience. Since the *CP* transgene confers resistance to plant viruses, the Environmental Protection Agency (EPA) in the USA defined it as a pesticide and therefore subjected it to the evaluation of "tolerance-levels in the plant". An exemption from tolerance was petitioned, and then granted, on the basis of the simple argument that "much of the papaya eaten in the tropics is from PRSV-infected plants" (Gonsalves *et al.* 2007; Susuki *et al.* 2008). In Mexico, PRSV infected papaya is extremely common on store shelves and acceptable to consumers; most, if not all, untainted fruit is destined to export markets. The specialized health subcommittee from CIBIOGEM would be the one taking this argument into consideration in the event of analyzing a petition for a Mexican GE PRSV-resistant papaya.

It is difficult to predict whether transgenic papaya could have the fate of GE maize in Mexico or, indeed, that of transgenic papaya in Thailand (Davidson 2008). Davidson's lively and detailed description of the turbulent process that led from an attempt at deregulating GE PRSV papaya to a countrywide moratorium on all field testing of GE crops, testifies to the vagaries and variety of political and social factors that have hindered the adoption of a promising technology in a country that had already developed a competitive biotechnology sector in the region (Davidson 2008).

Intellectual property rights (IPR)

IPR, generally designed as incentives for technological development, may represent major drawbacks to small farmers, restricting traditional farming practices such as saving and sharing seeds, and imposing new financial burdens (Fransen *et al.* 2005). Access to new seed could come to a halt due to royalty costs. Agri-biotech licensing has unique aspects that differentiate it from other technology-based intellectual property licensing (Cahoon 2007). The transfer of GE papaya in the US and in Thailand has been widely documented (Davidson 2006; Cahoon 2007; Gonsalves *et al.* 2007; Davidson 2008), and provides an essential starting point for developing appropriate licensing agreements in the event of the transfer of GE PRSV-resistant papaya from public research institutes to Mexican resource-poor farmers. Key issues will be to establish humanitarian clauses that preclude the payment of royalties in the case of small scale farmers and to set up appropriate mechanisms to prevent illegal commercial-scale abuse.

PUBLIC PERCEPTION OF GE PAPAYA IN MEXICO

In Mexico, the public perception on GE crops is divided, especially concerning food products. The main controversy in Mexico revolves around transgenic maize and the scenario for the introduction of other edible GE crops is, at present, unpredictable at best. Papaya, one of the cheapest fruits available all year round in Mexican markets, is highly prized as raw fruit and for preparing "smoothies", and has also found various uses in traditional medicine (Ross 2005); however, it does not have the connotations of maize as a national symbol. It would be hard to imagine, in the case of GE papaya, an equivalent of the non governmental organization ¨Sin maíz no hay país¨ ("There is no country without maize"), or unwieldy claims of biodiversity disasters by anti-GE activist groups. However, as has previously been mentioned, the introduction of GE papaya will entail the inevitable flow of transgenes to cultivated, feral and wild forms of *C. papaya* present in Mexico, and questions will arise concerning the reproductive fitness and potential threat to biodiversity of feral and wild forms harboring a virus sequence conferring PRSV resistance.

The development of a GE PRSV-resistant papaya by Mexican scientists in public institutions, targeted to small and medium papaya producers, may be expected to draw positive public attention and feedback as a home-grown technology addressing the livelihood of the poor. As in other developing countries, there is a higher level of confidence in national scientists that develop locally adaptable technologies than in government officials or imported technologies (Aerni and Bernauer 2006; Abdulkadri *et al.* 2007; Soleri *et al.* 2008). This is in sharp contrast with the situation in richer countries, such as France and other members of the European Union, where public opinion on GE crops reflects a deep mistrust not only of those who market the technology and regulate it but also of those that develop it (Fransen *et al.* 2005; Bonneuil 2008). Broader acceptance of GE crops under these circumstances may increase if the technology is perceived as something that truly addresses people's needs (Bonneuil 2008). In Mexico, actors and stakeholders of promising GE technologies should endeavor, on a case by case basis, to learn from these lessons and develop innovative transfer strategies that take into account at the outset the usually harsh economic and social realities of resource poor farmers.

CONCLUDING REMARKS

As the second worldwide papaya producer and top exporter, Mexico is poised to embrace GE PRSV-resistant papaya. Several technical and regulatory reasons favor the eventual adoption of this technology. Mexican scientists in public institutions have developed GE papaya and have the capacity to improve the technology using state-of-the art methodologies that would reduce some of the real and perceived risks associated with GE crops. The use of non-translatable genetic constructs for transformation should help reduce risks to human health and potential environmental impact. The diversity of the virus in Mexico has been documented, thus facilitating the ongoing development of transformation constructs for GE papaya with broad resistance to diverse PRSV isolates. The pertinent regulatory framework for GE organisms is now formally in place; more than 50 applications per year for experimental trials of various GE crops have been submitted to CIBIOGEM over the last four years (CIBIOGEM 1999b). Of these, 51 have been authorized and 90 are being processed. But there have been no applications for GE papaya. Why? Mainly for the same reason that led to the abandonment of the four applications for GE papaya that had been filed in 1997-8: lack of interest from the large producers that initiated the process. At present, large papaya producers in Mexico are content with crop management solutions to control the impact of PRSV in their fields. To them, GE papaya would only encourage new players to enter an already competitive market. In the case of small producers, GE PRSV-resistant papaya is an attractive solution to a yearly problem that increases production costs and reduces crop yields and fruit quality. However, resource poor farmers lack the necessary political force and organization, not to mention the pertinent technical knowledge, to advocate the transfer and adoption of GE papaya. This is highly reminiscent of the rise and fall of a Mexican project on virus resistant GE potatoes at the end of the previous decade (Chauvet *et al.* 2004; Pray *et al.* 2008). The *ex ante* study of the potential social impacts of GE papaya has given us valuable clues concerning who should benefit most from the technology – small farmers – and why large producers are averse to its promotion. But who should push GE crops from the research centers all the way to the farmer (a major pitfall of the potato project)? Scientists, regulators and sociologists should participate by actively taking part in the design and implementation of education and promotion campaigns as well as a continuous dialogue aimed at resource poor farmers and their crop requirements on the one hand, and at consumers and the general public on the other. Existing channels designed to strengthen the agricultural supply chain, such as the "Sistema Producto", must provide technical assistance to and defend the needs of small producers.

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