Experience with GMOs in Spain, the first country in Europe cultivating Bt-maize
Prof. Pere Puigdomènech

Pere Puigdomènech is the Director of the Centre of Research in Agricultural Genomics (CRAG) in
Barcelona and has been a member of the EU advisory group on Biotechnology and the European Science
Foundation’s expert group on Biology and Society. At CRAG model plants as well as cereals, fruit trees,
horticultural crops, and farm animals are studied. They also provide services in molecular methods such
as genotyping, genomics, proteomics, and metabolomics.

Puigdomènech focused his talk on the cultivation of Bt-maize (maize containing a gene from Bacillus
thuringiensis) in Spain, which has been successful in comparison to cropping of genetically modified
(GM)-crops in other European countries. He also explained the structure of the Spain’s National
Commission for Biosafety, which is composed by members of different ministries and scientific experts.
This commission regulates and provide public reports on field trials.

There are several reasons why Bt-maize has found acceptance in Spain. To start with, Spanish farmers
face stiff competition from other maize produces and there is a considerable and steadily increasing
import from other European countries and the Americas. Bt-maize was first introduced on the market in 1998
and is today mainly grown in two Spanish regions where the European corn borer (Ostrinia
nubilalis) causes problems. Today it accounts for about 30% of the total maize production and is used for
feed and industrial uses.

It is well known that the public perception towards GM-crops varies between different EU member states,
with Greece and Austria having a very negative perception. However, in spite of the large use of Bt-maize
in Spain, the public is not that sceptical. Puigdomènech lifted that one reason for this could be that the
general public in Spain are more confident in scientists than in other EU countries, and rank the
trustworthiness of scientists higher than e.g. NGOs. Furthermore, the ruling party in Spain, Partido
Popular, has taken a firm stand in favour of the technology. At the same time, the principle of co-
existence of conventionally and ecologically grown crops, together with GM-crops is well-established.
These factors together with the stiff competition farmers meet have led to that the cultivation of GM-
maize is fairly uncontroversial in today’s Spain.
A question was raised regarding the development of resistance and requirements for refuges with non-GM maize? In Spain it is recommended to sow refuges but because no region has more than 50% Bt-maize selection pressure is very low.

**Risk assessment of GM crops within EFSA and experience of GM field trials at Rothamsted Research**

**Prof. Huw Jones**

Huw Jones is the research leader in the Plant Biology and Crop Science Department at Rothamsted Research and a member of the Panel on Genetically Modified Organisms (GMO) within the European Food Security Authority (EFSA) based in Parma. At his Institute a genetically engineered wheat has been developed that emits (E)-beta-farnesene, which is a volatile compound aphids use as an alarm pheromone when attacked. The gene, originating from peppermint, has been transformed into wheat plants. This pheromone deters aphids from the wheat crop and, in addition, it attracts predators of aphids such as ladybird, lacewing and parasitic wasps. The idea is that the plant can defend itself, resulting in less need for insecticides. Because wheat is self-pollinated and not compatible with wild relatives it is highly unlikely to spread the genes to other plants.

The wheat has been tested in lab and in fact repelled the aphids more strongly compared to synthetically produced (E)-beta-farnesene. Last summer a first field trial was conducted at Rothamsted outside of London. Before the field trial a 60 day public consolation period was held, this time resulting in many letters of objection from individuals and anti-GMO organisations. However, Huw Jones thinks that a greater understanding and acceptance regarding GM-crops has emerged during the last year, maybe due to extensive and mostly positive media interest in the Rothamsted trials. In addition public acceptance has been greater probably because it is the first GM-wheat tested and that it has not been produced by one of the big multinational breeding companies. During the field trials an open letter was published and some Rothamsted scientists made a short information film to explain the research and ask the protestors not to destroy the trial which had a positive effect on the public’s and media’s attitude. The only incident at the site was a person that managed to breach the security and get into the field in order to spread organic wheat seed. But by that time the test crop was already well-established and the contaminating seeds could be distinguished and removed. The researchers at Rothamsted will repeat the trial in 2013 and publish their results of both trial years in a peer-reviewed journal.

The European Food Safety Authority (EFSA) works on a €77 million budget and use 167 scientific experts on 10 panels. EFSA is an independent scientific agency of the EC that carries out a risk evaluation of GMOs and publishes its opinion. This outcome requires approval by EU member states, often after protracted political discussion. The usual voting habits of the EU member states are that South and East EU tend to vote NO more often than other parts. So far 53 applications have been adopted by EFSA, and a further 60 are in process – of which about 50 are stacked events i.e. crops with combinations of different GM-traits. Most of the previous applications have been various herbicide tolerance or insect resistance traits but recently some new traits such as altered starch and fungus resistance (the Amflora and Fortuna potato varieties), thermo-stable maize for ethanol production, and soybean with reduced poly-saturated fatty acids are in the pipeline. The cost for regulation and risk assessment in bringing a new GM-crop to
the market is somewhere between 7-15 million USD. This is a staggering amount which effectively restricts activity in this area to big multi-national biotechnology companies.

The Amiga project: Assessing and monitoring the impacts of genetically modified plants on agro-ecosystems
Dr. Tina d’Hertefeldt

Tina d’Hertefeldt is a researcher at the Department of Plant Ecology and Systematics at Lund University and part of the Seventh Framework Program (FP7) financed program AMIGA; Assessing and monitoring the Impacts of Genetically modified Plants on Agro-ecosystems. She is a member of the board of the Swedish Ecological Society, Oikos, and the Swedish Board for Gene Technology.

Tina d’Hertefeldt focused her talk on practical GM-tests and communication. In the AMIGA program EU has been into regions to answer the question; can genetically modified crops have different effects in different parts of EU due to local environment? A lot has already been done for risk assessment and management. What are the EFSA decisions based on? AMIGA strived to simplify this document. In AMIGA, researchers will do practical test of ecological studies, look into post market environmental monitoring, and evaluate the economic impact with Argentina as an example country. The goal is to increase the confidence in guidance document and develop a robust risk assessment and effective post-market monitoring. The Bt-maize MON810 is used as a model crop with field trials outside Lund along with similar trials in Spain and Slovakia. Denmark and Rumania will also host maize trials in 2013. Amiga also includes studies on non-target organisms in potato, and a GM-potato resistant to late blight is grown in Ireland.

It is difficult to assess on how much effort is needed to sample insects enough to get good measures of non-target effects: How many samples over one season? When in season to sample? To which taxonomic level should insects be identified? In Sweden, there is a specific interest to investigate the presence of honey bees in the maize field, which is linked to the EU pollen verdict that states that honey may not contain any GM pollen. It has been important to inform beekeepers about when the maize would flower and a pollen trial on honey bees and bumble bees is also performed in the project.

Initially there was no interest to grow Bt-maize in Sweden because maize was such a small crop with no problems with the target pest, the European corn borer. However, increased maize cropping and climate change have brought the pest, not only closer to Sweden but signs of attacks in fields have been found on Öland and also outside Lund, and such a field is planned to be included in the next field season. The experience from the first field season shows that there is a strong need to customize the sampling protocol of non-target organisms so that it is possible to evaluate possible effects. The open communication about the trial is in line with the aim of the Amiga project and has been important in order to communicate why we planted the field trial. Findings of the first season will also be communicated back to the public.

Emerging techniques
Dr. Marie Nyman
Marie Nyman is Head of Division at the Swedish Gene Technology Advisory Board in Sweden and she talked about new techniques for plant breeding and GMO-legislation. She pointed out the fact that the biotech techniques regarded to result in a GMO are listed in the annex of the EU directive on genetically modified organisms (201/18/EC). These include recombinant nucleic acid techniques as well as heritable material prepared outside the organism and introduced in a host organism. Another annex to the directives lists exempted techniques, such as mutagenesis and cell fusions of plant cells from organisms which can exchange genetic material though traditional breeding methods. These techniques are exempted on the condition that recombinant nucleic molecules have not been used. Since some of these techniques creates site-specific mutations using nucleic acid molecules, one of the key issues is whether a e.g. synthetic oligonucleotide is a recombinant molecule or not. Parts of the EU regulation on those techniques dates back to 1983, which creates problems since molecular biological techniques are rapidly developing, and there are today several examples of techniques for which it is unclear if the end-result should be regarded as GMO or not. Consequently it is uncertain whether these should be regulated or not. Examples of techniques which are currently discussed are oligonucleotide-directed mutagenesis (ODM), site-directed nuclease (e.g. ZFN and TALEN), cisgenesis/intragenesis, grafting of non-GM scion on GM-rootstock and vice versa, reverse breeding and synthetic genomics. A working group to evaluate these new techniques with members from the EU states was set up after a proposal from the Netherlands 2007. Their task was to evaluate a list of techniques, provided by the commission, in the light of the definition of GMO/GMM, the techniques listed in the annexes and the most recently available scientific data. The working groups report was distributed to the member states competent authorities in the beginning of 2012. According to a report from DG Joint Research Center the end-product of many of these techniques cannot be detected and a method of detection is a requirement in the legislation.

The largest uncertainty around new breeding techniques is of course whether they are going to be classified as GM or not by the EU, a decision which will have large consequences on the costs associated to risk assessment and registration. In general, Marie Nyman noted, science moves forward faster than the EU regulation. The crop closest to the market based on such a technique is Cibus’ herbicide tolerant rapeseed. This crop is not considered as being genetically modified in the US, and interestingly not in the UK or Sweden either.

**Risk assessment and regulation of new breeding techniques**

**Dr. Frank Hartung**

Frank Hartung is a researcher at the Julius Kühn-Institut (JKI) Quedlinburg, Germany and member of the EPSO-Working Group on Agricultural Technologies and member of the EFSA working group on the risk assessment of plants developed through new techniques.

Frank Hartung continued to talk about risk assessment and new breeding techniques with a deeper focus on the actual molecular methods used. He started off with reminding the audience that today 160 million hectares GM-crops are grown worldwide by no less than 16.9 million farmers. As a member of the EFSA working group on risk assessment of plants developed by new techniques he has examined these in the context of the European GM legislation. A final report was presented in February 2012. Frank Hartung especially stressed different techniques for site directed nuclease (SDN). Organisms as an outcome of
some of these are, suggested by the working group, not to be considered as genetically modified; among
these are oligonucleotide-directed mutagenesis (ODM) and certain zink-finger nuclease methods if
recombinant DNA is not used (for more details, see presentations at www.slu.se/mistrabiotech). In
comparison to the introduction of recombinant DNA or classic mutagenesis these new breeding
techniques facilitate more precise mutations, transfer and integration of DNA, and have less side-effects.
It is also possible to avoid the usage of selection markers. In fact, transgenes and non-transgenes cannot
be distinguished after the events, which is a pre-requisite for monitoring and regulating GMOs. In
addition many of the new breeding techniques are more cost-efficient also at the initial developmental
stages compared to other breeding techniques.

Marie Nyman’s and Frank Hartung’s presentations led to a discussion in the audience on the currently
very technique-based regulation within the EU and whether it would not be more appropriate to regulate
and risk assess the end-product irrespective of technique used.

Policy of Federation of Swedish Farmers on GM plants
Jan Eksvärd

Jan Eksvärd is environmental manager at the Federation of Swedish Farmers (LRF), and he began by
pointing out that a sustainable agriculture both needs to deliver more food to the plate and reduce
environment impact. Social, ecological and economic factors have to be weighed in. Some of the future
challenges are that 50-30% of all food is lost on its way to the plate, how to use the available land for
food, feed, fuel or fibres and adaption to climate change with 5 month longer growing period.

Jan Eksvärd expressed that the EU approval system on GMOs is too expensive, reducing development
and competition among breeding organisations and that knowledge and companies in the sector are
leaving the EU. Besides new cropping management practices, agriculture needs crops and varieties with
new appropriate properties for the Northern climate to meet our challenges. Focus should be on how to
develop a more sustainable agriculture. All old and new techniques are probably needed. Farmers want
new varieties to be safe so all new properties should be tested in an approval system that gives a safe
enough result, is fast, cheap and encourages competition among breeding companies and institutions. Jan
Eksvärd also believed that the current debate which focuses on for or against GMOs need to be held in the
broader context of sustainable development and new properties independent of breeding method.

A review system should be developed that focuses on sustainability and health issues on a system level,
independent of breeding technique. Investigations could differentiate depending on type of new
properties, earlier experience, gene mapping and used technique. This could initially work in parallel with
the GM review system.

LRF has a general policy for genetically modified products stating that they e.g. should contribute to a
sustainable development, be evaluated on the basis of precaution, follow the values of farmers and
consumers, be labelled, and allow the coexistence with non-GM cultivars. The debate around GM-crops
should be conducted in an open manner.
After the presentation the question who should take the lead in taking the debate to the next level arose. To this Jan Eksvärd pointed out that farmers and scientists to a large extent have similar views on what is needed, not to forget that consumer trust is a key for success. The question should be broadened to new properties for sustainable development and that both old and new techniques will be needed. With an approving system that focuses on new properties, not only the breeding industry can develop but also the debate can be held in a broader context.

Public acceptance of different biotech and GM-technologies
Prof. Sven Ove Hansson

Sven Ove Hansson is Head of the Division of Philosophy, Royal Institute of Technology, and Program director at Mistra Biotech, at SLU. He is also President of the Society for Philosophy and Technology.

From one point of view GM crops have been very successful with an incredible increase during the last 20 years. There is no other example of an agricultural practice adopted so fast. Of the food sold in North American grocery stores, 70% contains at least some GMOs. At the same time, the technology has encountered strong resistance in many European countries, but from a global perspective this stand against GM-crops can be seen as European “exceptionalism”. But there are also other techniques that encounter public resistance, even if few quite as much as GM.

What are the characteristics for such technologies? If there are direct personal advantages, a technology will be accepted even if ‘dangerous’. An obvious example is the internet (which e.g. enables pedophilia, terrorism). Another example is mobile networks where the public is usually more concerned about the radiation from base stations than from mobile phones, which are perceived to be very useful in everyday life, in spite of the fact that the base stations give rise to lower doses of (non-ionizing) radiation than the mobile phones. The same is true in biotechnology, where there is little public resistance against recombinant DNA if used for therapeutic purposes.

Members of the public - irrespective of political views - are generally suspicious against technology good for governments or big companies, and show low tolerance to techniques benefiting these parts of society. Other aspects that can raise concern in the general public is the notion that humans should not play God, which is an example of issues not linked to risk but rather to ethics. This and other issues linked to belief or religion can be classified as “world-view issues”.

Human beings tend to treat new technologies as a matter of risk, which might be problematic. In the case of GM-crops it would be wise to take precautionary measures only for some types of genes. But it is hard to argue that this should be inferred in general for all genes and GM applications. Still, the technique as such is considered dangerous.

Risks are often perceived by the general public who then express their fear, but it is important to distinguish that concerns may have different origins. It is extra difficult when public concern is not linked to true risk introduced by a technique.
And sometimes even experts might be wrong! For example experts in nuclear science in the 70’s (when also the concept of GMOs first evolved) calculated that one melt down would occur in every 1,000,000 reactor years. The result to date is 5 melt downs in 50,000 reactor years, which gives a frequency of 1/10,000 not 1/1,000,000. Most technologies are connected to some sort of risk. The best solutions are those that make accidents impossible (inherent safety), not only reduce their probabilities.

The goal should be “transparent safety”, where it is easy for non-experts to ascertain safety measurements taken and make these readily understandable.

With respect to GM-crops the following should be considered:
1. We should distinguish between different GMO applications; all GMOs can’t be treated alike
2. Personal advantages such as health benefits or price with GM-crops should be highlighted.
3. What is benefiting big companies and governments or farmers and consumers should be distinguished, highlighting farmer focused advantages.
4. Find better ways to address world-view issues
5. Specific examples where transparent safety can be applied should be identified.

After the presentation the question of the influence of price on GM choice among consumers was raised in the audience; generally people are not willing to trade off safety for price.

Panel discussion

Q: What will be the situation for GM in Europe in 20 years?
Jan: No difference, legislation has to be replaced. GM feed will still be imported.
Huw: No dramatic changes in legislation. For public confidence, risk assessment is needed for the specific products if GM crops are to exist. Importation of GMO will continue but cultivation of GMOs will be slower; but new attempts to introduce GM-crops on a member-state by member-state basis might occur. There is an EU proposal of non-cultivation clause for member states over-ruling scientific evaluation and recommendations.
Tina: Real needs should be put in the first place and be communicated well.
Marie: Slight optimism even without a new legislation and a new legislation will be initiated.
Frank: Better than today because of worldwide spreading of GM-food and feed.
Pere: New traits that benefit people might appear, like the golden rice. Traits that are viewed as positive could improve status. Economical down-turn in Europe might lead to focus on more pressing questions other than GMOs. Communication is still important.

Q: What measures could be taken to achieve a more positive future?
Jan: There should be a focus on properties of crops independent of breeding technique.
Tina: We should ask ourselves which ecosystems services we need rather than “how can this method solve the problem?” GM should be approached as a whole package with advantages and disadvantages.
Jan: I do not agree, focus on properties independent of breeding technique instead.

Q: Companies have now withdrawn from Europe; what will the funding be in the future?
Huw: No big biotech companies left in Europe. Only academic research today and this is very small since route to application/market is difficult and expensive. Many scientists in applied biotech have left this research field or left EU. Smaller breeding companies cannot afford the costs of R&D and regulation. Still Europe has become a consumer of GM crops.
Jan: There is not much time; present legislation need to be replaced.

Q: Surprises might occur and play a role, like the BSE crisis for example. We need to be humble also when we talk about properties.
Jan: Agree, but we should not get stuck in present situation.
Huw: Legislation based on processes has to continually chase new technologies all the time and will constantly lag behind; and will as a consequence become illogical. Better to evolve a regulatory framework based on trait/product.
Pere: Properties a possible way out. But environmental arguments are difficult since targets are complicated.
Tina: Money to protect biodiversity and function has no clear links. We need to evaluate all crops not only GMs, which crops advances ecosystems services and which do not.

Q: Third world will bring technology forward, and break the viscous circle in Europe. Such a change could influence NGOs and make them realize that they should focus on larger issues. GM is also a question of European protectionism. Sometime in the future even European skeptics can change target if progress in the developing world goes well.

SO: That would be an unusual technology-transfer from Africa to Europe, usually it is the other way round!

Q: Who should drive the public discussion on plant biotech inventions forward?
Frank: Bring up something people are interested in. It is hard for scientists to reach the heart of people.
Jan: We should communicate together to create trustworthiness; farmers, scientists, environmentalists.
Huw: Scientists should share the platform together with farmers and NGOs complimenting each other. There is a lack of scientific understanding among European politicians.
Tina: Risk assessment; clear risks are identified and we need to communicate the unattractive areas linked to GM as well. And acknowledge also areas that are not acute risks.
Marie: Developing world might be the way forward. Many people are surprised when they hear about the state in EU.
Pere: Who is an expert? Experts can also come from industry. Being on different boards is time consuming and does not much for your career. Who should we choose? Scientists will have an important role there.

Comm.: Legislation lags behind at the same time as the in development rushes. Now with even more powerful tools at hand, scientists should be even more pedagogical towards to the general public not to increase worries. It is a danger that new breeding technologies will be regarded only as a way for scientists and companies to bypass legislation. Biosafety legislation is needed, not a technique based one.
Om PlantLink och Mistra Biotech:

Plant Link is an alliance between Lund University and the Swedish University of Agricultural Sciences in Alnarp (SLU Alnarp). Our mission is to stimulate and coordinate plant research and higher education in Southern Sweden. We strive to increase the interest and competence in molecular plant science and we want to create an environment that promotes research, innovation and a dynamic interaction between the universities, private companies and the general public. Plant Link has financial support from the Skåne Regional Council (Region Skåne). More information at www.plantlink.se

Mistra Biotech is a research programme that started in the beginning of 2012. The research is focused on different aspects of the use of biotechnology in agriculture and involves scientists from several disciplines. Most researchers work at SLU but researchers at KTH, Lund University, Aarhus University and Roskilde University are also involved. The goal for Mistra Biotech is to contribute to sustainable agricultural and food production, from an environmental, social and economic perspective. The programme is funded by The Swedish Foundation for Strategic Environmental Research (Mistra) and SLU. More information: www.slu.se/mistrabiotech