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ENGAGING WITH UNCERTAINTY AND RISK IN AGRICULTURAL BIOTECHNOLOGY REGULATION: DELIVERING SAFETY AND INNOVATION

Final Report

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1. Introduction

The project *Engaging with Uncertainty and Risk in Agricultural Biotechnology Regulation: delivering safety and innovation* was funded jointly by the Economic and Social Research Council (ESRC) and Syngenta. It focused on the EU regulatory process for assessment of the environmental risks associated with the introduction of GM crops in the European Union. A full description of the aims, methods and results is included in Annex 1. This paper summarises the background analysis conducted by Innogen along with the research outcomes, and proposes a new approach to governance and engagement in relation to innovation for agricultural biotechnologies in the EU.

1.1 The Policy Gap

A starting point for this project was the identification by Syngenta staff of a 'risk assessment-policy gap' in the regulation of GM crops in the EU. Such a gap was discussed by Evans *et al.* (2006) in the context of the UK contaminated land regime. This gap is related to the absence of operational definitions of environmental protection goals on the basis of which risk assessors can determine when an endpoint has been reached that satisfies the regulator's requirements for a low probability of harm (Garcia-Alonso and Raybould, 2013). Dealing with the gap would require a political debate to set out societal goals, regulatory guidance to determine application and a legal debate to establish precedence. Ensuring stakeholder input during problem formulation to achieve consensus on risk management goals and to improve accountability is suggested as a means to mitigate this gap, although Evans *et al.* recognise that citizens are not always in agreement over risk management objectives and indeed there can be substantial disagreement even among 'pro-environment' groups. Ambiguous policy statements are thus in many cases accurate representations of societal objectives.

Raybould and Poppy (2012) have proposed that this gap explains why accumulating ecological research showing negligible environmental risks from the use of GM crops has failed to expedite regulatory decisions about cultivation approvals for these crops in the EU. However, identification of the nature and causes of a policy gap is not necessarily a prelude to closure of that gap. If, as Evans *et al.* (2006) claim, societal consensus is a necessary prerequisite to the definition of clear operationally defined policy objectives, and thence to regulatory decisions based on scientific evidence, the European regulatory system for GM crops may remain in its current unsatisfactory state for the foreseeable future (IRGC, 2009). Indeed ambiguity surrounding policy objectives seems increasingly to be the norm across a wide range of policy fields, particularly in the EU.

New risk governance and regulatory approaches will be required if the EU is to retain a role in the development of a wide range of technologies that will be part of the global bio-economy in the coming century. These new systems will need to be better adapted to the opportunities presented by 21st century science, and to be robust, flexible and democratic in the face of societal pressures while continuing to ensure safety for people and the environment.

1.2. *Engaging with Uncertainty and Risk in Agricultural Biotechnology Regulation*

Innogen research has covered these issues from the perspectives of policy and innovation interactions in the development of GM crops (Tait and Chataway, 2007; Chataway *et al.*, 2008; Tait, 2009b; Tait and Barker, 2011), and of synthetic biology (Tait, 2009a; Lowrie and Tait, 2011; Tait, 2012). Castle's recent work on herbicide tolerant canola in Canada has also helped to reduce the uncertainty around the agricultural and environmental benefits of adopting these crops, creating space for clearer policy questions (Gusta *et al.*, 2011; Smyth *et al.*, 2011).

Underlying themes in all these studies are the treatment of uncertainty in debates about agricultural technologies, and related questions about the role of scientific expertise

relative to lay judgements in policy decision making. Collins (2008) and Collins *et al* , (2010) have distinguished between the role of scientific expertise in policy making and that of non-expert citizens, making a case for greater separation of "... the oil of politics and the water of expertise ... at every institutional level" and arguing that this is "...essential if the integrity of scientific advice, and the very idea of science, is to survive". Collins also recognises that many choices will ultimately be based on political judgements but claims that the proposed separation will clarify the nature of those political choices.

Pielke (2007) has focused on the roles adopted by scientists in advising policy makers: the pure scientist, the science arbiter, the issue advocate, and the honest broker. He notes that all four roles are relevant and useful in a democratic process, but he also points to the existence of 'stealth issue-advocacy', which allows an adviser to claim to be "...above the fray, invoking the historical authority of science while working to restrict the scope of choice", a role that has been taken up very effectively by some social scientists and has had a strong influence on the governance of GM crops in the EU (Mayer and Stirling (2002); Millstone *et al.* (1999); Von Schomberg (1998); Wickson and Wynne (2012)).

This project will build Pielke's and Collins' insights into the Innogen Institute's research on Adaptive Governance of Innovative Technologies (AGIT) and Constructive Stakeholder Engagement (CSE), in the context of EU regulatory systems for GM crops and, potentially, synthetic biology.

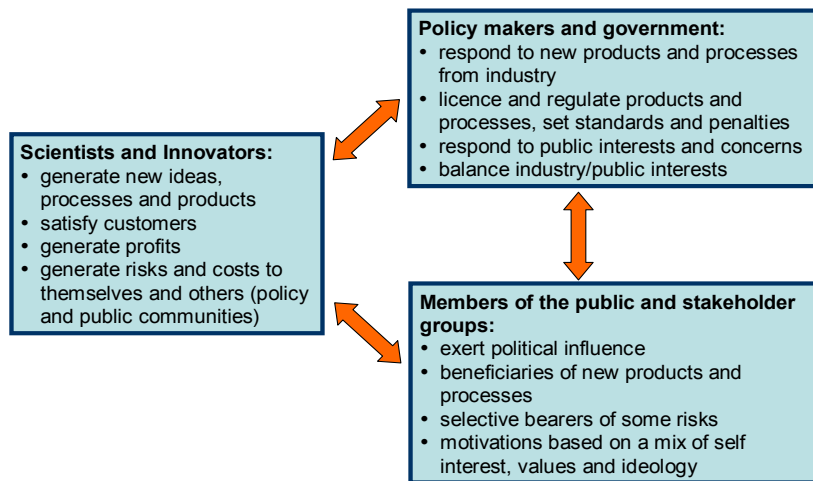
2. Research Framework for the Project

The Innogen Institute's research adopts a triangulation approach (Figure 1) that considers how the fate of life science products and processes, in particular their ability to reach practical application in a commercial or public sector market, depends on the interactions among three constituencies: (i) scientists/innovators; (ii) policy makers and government; and (iii) citizens/stakeholder groups. Our research methods consider in detail the behaviour and decisions of actors in each of these constituencies, with an internal focus on innovation business models and value chains and an external perspective on the actions and influences of the other two constituencies. This enables us to locate pressure points that could deliver change or realignment in overall system behaviour, for example so that innovation could take place more rapidly and more cost-effectively without lowering safety standards.

This project has focused mainly on the interactions within and between policy makers/government (based on the Adaptive Governance of Innovative Technologies (AGIT) approach (Tait and Chataway, 2007; Tait, 2008, 2009, 2012; Tait and Barker, 2011)), and public/stakeholder groups (based on the Constructive Stakeholder Engagement (CSE) approach (Bruce, 2011; Tait, 2009b)), as they impact on the third set of constituencies - scientists/innovators.

The project incorporated Syngenta's data, insights and expertise and Innogen's background analysis and research approaches to characterise the problems arising from current EU regulation of GM crops and, potentially, future regulatory approaches for new research areas such as synthetic biology. We considered how future governance of advanced agricultural biotechnologies could be based more effectively on scientific evaluation of product risks and benefits and have suggested how firms and policy makers could engage on a more balanced basis with civil society stakeholders to enable safe and responsible delivery of innovative products.

Figure 1. Innogen Centre approach to life science innovation analysis



3 The European Regulatory System for GM Crops.

3.1 The current regulatory system

As described in more detail in Section 2 of the Annex to this paper, the EU regulatory system for GM crops has evolved since the 1980s as a precautionary, process-based approach, in contrast to that of the USA which has been more strongly evidence- and product-based. As Tait and Levidow (1992) demonstrated when the regulatory system was being set up, these very different approaches could have had broadly comparable impacts on the development of GM crop technology on either side of the Atlantic, depending on how they were implemented by regulators. Both could have been equally vulnerable to the politicisation that has so far occurred mainly in the EU.

We focused on the following risk-related requirements placed on applicants wishing to introduce a GM crop on the market for cultivation in the EU by Directive 2001/18/EC: an environmental risk assessment; post market monitoring plans; provision of information to the public; labelling and traceability provisions at all stages of development; information on identification and detection of the GMO.

The European Food Standards Authority (EFSA) is the lead agency in managing the application process. For cultivation applications, it allocates the company's application for regulatory approval to one of the European national competent authorities (CAs). At this stage, the CAs of other EU member states have the opportunity to ask further questions or to ask for clarification of specific points in the dossier. Once the dossier has been given a positive assessment by EFSA, the European Commission drafts a decision which is presented to the Standing Committee of the Food Chain and Animal Health of Member States (Standing Committee) which votes on the decision. Under the old system, in the absence of a qualified majority in favour of that decision, the decision would be passed to the Council of Ministers and, if there was still no qualified majority in favour, would be passed to the European Commission after which the Commission had to act within a specified period. Under the current system, in the absence of a qualified majority in favour of that decision, the decision would be passed to an Appeals Committee with the power of scrutiny. If the Appeals committee rules against the Commission Decision, the

Commission must abide by that ruling (<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2011:183:0013:0016:EN:PDF>)

To date the fate of GM crop cultivation applications in the EU has mainly been that, following a positive opinion by EFSA, the required qualified majority has not been obtained from the Standing Committee, leading to a stalemate as the key actors beyond that point in the process are unwilling to take the political responsibility for a decision that would follow the European Commission's recommendations. Recently the agro-biotechnology company DuPont Pioneer has sued the Commission over delays in decisions about cultivation of 1507 maize¹.

The risk assessment requirements of the EU regulatory system are relatively standard components of risk- and evidence-based regulatory systems internationally. However, the problems for EU governance of GM technologies arise in how the risk related requirements are elaborated and the subsequent fate of the EFSA dossier following delivery of EFSA's advice. The expectation in the early 1990s was that, as experience in growing GM crops accumulated, the level of precaution applied by the regulatory system could gradually be relaxed. However, the reverse has been the case and in the intervening period the EU regulatory process has seen a steady increase in the level of precaution, with frequent revisions introduced in a capricious fashion in response to political pressures from vested interests, mainly environmental advocacy groups and political parties.

3.2 Contributory factors in development of regulatory systems for GM crops.

Innogen's research has noted a significant trend in the development of regulatory systems for life sciences since the 1980s, when a new policy agenda emerged, supporting a move away from the previous *government* approach based on top-down regulation to a *governance* approach with a much increased role for non-government actors in policy-making (Lyall and Tait, 2005). We use the term governance here to cover both the regulatory system that ensures safety and efficacy of products and processes and the political system within which it operates.

This policy shift in the 1980s enabled the emergence of an advocacy coalition (Sabatier and Jenkins Smith, 1993) that campaigned very successfully against GM crops, so that the regulatory environment in the EU, and also in United Nations (UN) conventions such as the Convention on Biological Diversity (CBD) and its subsidiary protocols, particularly the Cartagena Protocol², remains extremely restrictive in the context of GM crop developments. The EU regulatory system, supported in some contexts by that of the UN, is unlikely to be compatible with a profitable European industry sector producing GM crops, and development and production of GM crops are now increasingly based outside Europe.

The above policy shift, linked to the coincidental adoption of the precautionary principle, undermined the role of scientific evidence in regulatory decision making, replacing it with often alarmist conjecture supported by media campaigns. The ideologically motivated advocacy groups that dominate the GM crops area are reluctant to change their opinions in the face of evidence that challenges their fundamental beliefs (Tait, 2001) and have so far been able to maintain political resistance to any attempt to adapt EU GM regulations to accommodate the increasing amount of evidence that these products offer alternative or significant additional benefits compared to the technologies they would replace.

¹ http://europa.eu/rapid/press-release_MEMO-13-960_en.htm

² The USA is the only major country that is neither a Party nor a Signatory to the CBD; Argentina, Canada, Japan and South Africa are Parties but not Signatories to the CP; and Australia and the USA are neither Parties nor Signatories to the CP.

Thus in the EU, the adoption of a governance approach has led to steady erosion of the quality of the evidence base to support regulatory decision making (Tait and Lyall, 2005). More generally the systemic interactions among the three constituencies in Figure 1 have become increasingly dysfunctional in the context of the development of agricultural biotechnology, with no simple or obvious mechanisms for resolution of the impasse.

4. Experience of two GM Crops (Bt11 maize and GA21 maize (hereafter referred to as Bt11 and GA21 respectively)) in the European Regulatory System

We analysed Syngenta data on two GM products, Bt11 and GA21 maize, in their passage through the European regulatory system, in order to generate evidence relevant to its current state and to identify how its operation could become more adaptive to evidence of its risks and safety.

The case studies, described in detail in the Annex, explored the nature of the relationship between changes in scientific uncertainty and the role of regulatory science in evaluating the risks of GMO crop cultivation. We also considered the nature of the precautionary political overlay that has essentially stalled the approval of these products. In the case of Bt11, for example, the scientific evidence and level of uncertainty about potential environmental impacts has changed substantially since the original application for cultivation was submitted in the late 1990s. Yet, this has so far proven insufficient to achieve a final decision. The Bt11 product is unusual when compared to other GMOs, including GA21, in terms of the approval process, since the initial application submission predated the existence of EFSA, so the product has been subject to a number of different regulatory regimes and has had to adapt to the emergence of new regulatory guidelines and protocols.

The GA21 case study revealed two main challenges facing GMO cultivation in Europe. First, the lack of agreed and workable parameters as to what are considered sufficient and necessary data to satisfy risk assessors, despite the fact that there are agreed upon methodologies and a scientific process. Second, a lack of agreement on what is sufficient within studies to demonstrate safety and minimize risk. These challenges were reflected in the responses and questions posed by EFSA, as well as the questions and objections from member country CAs.

Both case studies also highlight the long timelines for approval, which have cost implications, despite time limits imposed by EFSA. This was evident in the GA21 case study, where the 'clock stops' when questions are submitted through EFSA by member states.

Our conclusions from the case studies can be summarised as follows:

1. The political constraints placed on the approval process have so far made it impossible for the EFSA positive scientific opinions about GM crop cultivation in the EU to be followed through in practice. Where member states raise reference questions on points that Syngenta has already answered, EFSA nevertheless sometimes requests more information or additional data from the company. Thus, the parameters for good and sufficient evidence for risk assessment are not always clear and are often shaped by politics. A summary and explanation of comments/questions posed by member states for both case studies is presented in Table 1 below.
2. EFSA and many CAs often blur the boundaries between the science of risk-assessment and scientific research. Thus in both case studies additional data or research were regularly requested that were not directly relevant to risk assessment. Consequently, there were no clear endpoints to the risk assessment process. The initial scientific opinion of EFSA on Bt11 in 2005, for instance, should have represented an endpoint in regulatory decision-making, if risk-assessment

has been the primary objective. However, since Bt11 has now been in the system for 17 years without a final decision, this has clearly moved beyond a risk-assessment process.

3. The political process appears to be considerably more restrictive than the regulatory process. Regulation can be long and complicated but should, if done correctly, produce an outcome. In the cases of Bt11 and GA21, the political process remains an indefinite barrier to introduction of these products in the EU.
4. Finally, given that both case study products have already been cultivated in many countries with no reports of adverse effects, this can be seen as indicating an absence of harm for both products, once again raising the question of what constitutes sufficient evidence of safety for EU regulators. The lack of operational definitions of terms such as harm and safety makes it easy to delay EU decision making by pointing to lack of evidence without specifying explicitly what evidence is being sought or what criteria and standards are required to be met.

We can conclude from these case studies that GM applications face (i) a set of normative positions attempting to block the process of approval, and (ii) a lack of parameters specifying what are sufficient data and what issues should be placed on the table, thereby potentially extending the regulatory process indefinitely. At present, there is no clear sign that definitive decisions are being contemplated for these issues.

Table 1. Total questions/statements from CAs

Member Country	Total questions/statements (GA21)	Total questions/statements (Bt11)
Austria	25	5
Belgium	4	10
Denmark		3
Finland	1	3
Germany	31	19
Hungary	2	
Ireland	2	1
Italy	1	14
Norway	6	
Spain	2	1
Sweden	4	10
Netherlands	2	3
UK	4	4
Total	84	73

In the case of Bt11, of the 73 questions/statements submitted by member states, 13 were simple reference statements, 2 were explicitly negative statements, 41 requested more data or clarification of data and 17 challenged the appropriateness or relevance of the scientific studies recommended by EFSA³. Germany and Austria were the two countries that submitted the most objections. The principal objections (relating predominantly to the environmental risk assessment (ERA) were the potential adverse effects on soil

³ These challenges were not considered relevant or sufficient by EFSA

organisms and arthropods, and the long-term effects on the environment of the Bt-toxin, which is contained in the product.

For GA21, of the 84 questions/statements submitted by member states, 10 were statements referring to other studies or data the member CA thought relevant in its analysis or of which it thought Syngenta and/or EFSA should be aware; 5 were negative statements disagreeing with some element of Syngenta's submission; 26 were questions or statements requesting more data or clarification, delivered in a neutral tone (i.e. not questioning the relevance or appropriateness of Syngenta's study, but asking for more information beyond that submitted); 43 directly questioned the appropriateness or relevance of Syngenta's studies or of its conclusions based on the study descriptions/data submitted; again most were not considered relevant by EFSA. As in the case of Bt11, Austria and Germany were by far the most critical.

5. Adaptive Governance of Innovative Biotechnologies

5.1 The Governance agenda and EU regulations

The new governance agenda adopted by European politicians in the 1990s has taken a highly precautionary approach to dealing with uncertainty, particularly for agricultural biotechnologies. This, coupled with upstream public engagement that sought to give more power to the voices of ordinary citizens in making decisions on all aspects of innovation from funding of the basic science to product approval (Wilsdon and Willis, 2004) has contributed to the current stalemate in EU decision making on GM technologies.

The social science field of Science and Technology Studies (STS) has played an important role since the 1990s in channelling public responses to GM and other novel biotechnologies into decision making on science funding and product development. Academics working in this area have undertaken much of the research on upstream engagement and have contributed significantly to the development of government policies nationally and internationally (Mayer and Stirling (2002); Millstone *et al.* (1999); Von Schomberg (1998); Wickson and Wynne (2012).

This approach has been at the expense of a broader societal consensus that could have generated agreement on the nature of relevant harms and benefits and then balanced the risks and opportunities arising from agricultural biotechnologies. As noted in Section 1.2 above, this is the kind of process that would be required to address the question of closure of 'the policy gap'. The current situation has thus meant that the regulatory system has been unable to adapt to new information about the safety of products, to allow European farmers to make choices in the market place about whether to grow GM crops, and citizens to choose freely whether to purchase GM food products.

5.2 The Adaptive Governance of Innovative Technology (AGIT) Approach

The AGIT approach being developed by the Innogen Institute has been designed to avoid this kind of systemic impasse and also, once such an impasse has arisen, to enable a more balanced outcome to emerge over time. It is adaptive in the sense of being able to respond to new knowledge about the properties of products and the innovation ecosystems within which they will be developed and also in understanding how existing regulatory systems could be modified to enable more innovation and more radical innovation to emerge from current research without jeopardising standards of safety and efficacy.

Section 3.1 distinguished between the precautionary, process-based approach adopted for GM innovations in the EU and the product-based approach in operation in the USA. However, this product / process distinction now appears somewhat simplistic and out-dated. The nature of a product and the process by which it is developed will be relevant at different stages of the innovation path for different types of innovation and the challenge is to select the most appropriate criteria for regulation of each class of innovation as it

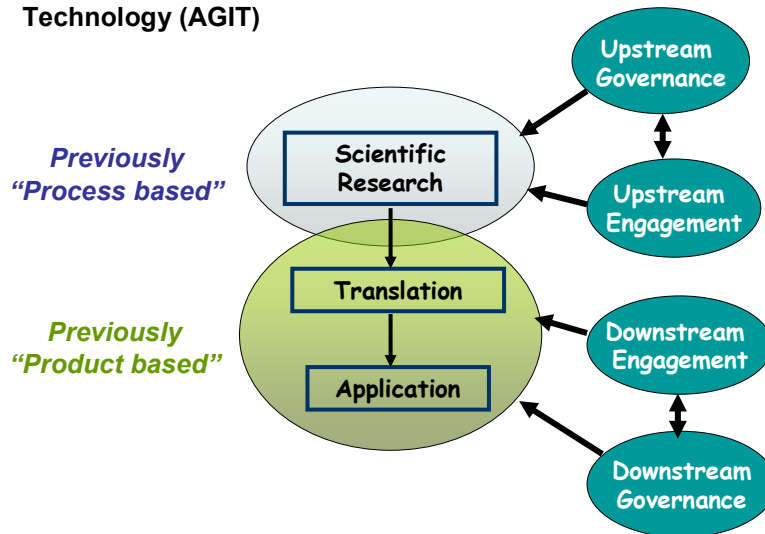
emerges from basic research and at different points in its development. The AGIT approach builds on the body of research on upstream governance of new technologies arising from the STS research community and extends it to be more adaptive in the context of new knowledge and experience, alongside a more constructive approach to stakeholder engagement (Figure 2).

Innogen's AGIT approach could be a basis for progressing to more effective risk management of agricultural biotechnologies. The core perspective is that of the companies and scientists involved in the development of new technologies (Chataway *et al.*, 2006), as they are translated from scientific research to real world applications. These are the activities conducted by science and innovation communities as they are affected by policy makers/regulators and by citizens and other stakeholders, i.e. the other two constituencies that form the triangle (Figure 1). The translation process involves two overlapping contexts, presenting different policy and engagement challenges and requiring different policy and engagement approaches (Figure 2).

- The **upstream** area at the top of the diagram covers the early stages of scientific research or translation, before it is clear what the exact nature of an innovation will be, when it will reach a market place, or what the relevant harms and benefits (or risks and opportunities (the latter defined as size of benefit x likelihood of benefit) will be. In this context, engagement and governance should focus on the novelty of the research processes being developed (GM in the 1980s or synthetic biology today) and any hazard that might be demonstrated by the process itself, rather than the still-unpredictable features of the final applications.
- In the **downstream** area, innovations in later stages of development will be relatively well characterised, including understanding of their potential benefits and the likelihood of any harmful effects (GM crops today), and conventional product regulation should be the usual mode of policy action, focusing more on the nature of the products themselves and less on the process by which they were developed.

Different issues arise, and different governance guidelines are appropriate, for these two contexts. Also, engagement with members of the public and with other stakeholders should take on different characteristics at each stage leading to different forms of stakeholder influence on governance processes (see Section 6). Likewise, the nature and degree of uncertainty changes as an innovation moves from research to translation to application. Upstream the main uncertainty is about whether the science can be made to work and what kinds of innovation are likely to emerge. Downstream uncertainty will be more resolvable by basic research that characterises the risks and opportunities of the various innovations. The governance approach adopted needs to be able to accommodate and adapt to such changes, particularly at the junction of the upstream and downstream processes in Figure 2. Any regulatory or governance approach put in place as part of upstream governance needs to have a specifically designed capacity to be adaptive in the face of new information that emerges in the translation process and in actual use.

Figure 2. Adaptive Governance of Innovative Technology (AGIT)



5.2.1 Upstream governance

For governance of research processes themselves and of products in very early stages of development concerns often relate to uncertainty about the nature and impacts of future products and processes with a stronger focus on ethical questions than for most well characterised products. In such cases, policy makers are struggling to keep pace with scientific developments and in some cases are attempting to leapfrog ahead of the research itself involving both upstream regulation and upstream engagement.

In implementing upstream governance, it is generally desirable to refrain from imposing regulatory constraints on development of new products and processes until there is good information on the nature of their benefits and risks, i.e. as far downstream as possible. However, pressures for more upstream regulation and governance can arise from investors who are reluctant to invest in new technology until they know what will be the nature of future regulatory systems. Likewise citizens who, as part of an upstream engagement process, are consulted about innovative science and technology in the very early stages of development often want to be reassured that it will be developed within a strong regulatory framework to ensure safety and/or delivery of public (as opposed to commercial) benefits.

Policy makers should, however, be more aware of the impact of their decisions on innovation futures. The nature of a governance approach chosen early in the development of new products can profoundly affect the innovation potential of entire industry sectors and indeed the capacity of countries and regions to compete in global markets. There is a history of decisions taken in early stages of product development, that are then difficult to change, and have unforeseen and counter-productive outcomes, particularly where regulation has been designed to reassure public opinion or to forestall perceived ethical concerns based on extreme interpretations of the precautionary principle (Tait, 2008). For example, if GM crops had been regulated from the earliest stage of development as if they were new crop varieties rather than as if they were more akin to pesticides, some would have been developed initially by seed companies rather than agrochemical companies, with a range of different first generation products and possibly with very

different European public attitudes to the technology. GM crops were a disruptive, path-breaking technology⁴ for the agrochemical industry sector but would have been easier to take to market, and with a different set of first generation technologies, where they had been developed by seed companies (Tait, 2007).

The following upstream guidelines are suggested for Adaptive Governance of Innovative Technology:

1. When considering which regulatory precedent is most appropriate for a newly emerging technology, a useful ground rule would be to choose the regulatory system in operation for the industry sector for which the innovation is path-dependent rather than one for which it is path-breaking (Tait, 2007).
2. Ensure that governance or regulatory decisions that are made very early in the development of innovative technologies have the capacity to be adaptive, i.e. retain scope for future modification of policies and regulations as more is learned about the opportunities and risks of a technology (Tait, 2009).

5.2.2 Downstream regulation

For products whose properties are well characterised, for example the GM crops available for use in non-EU countries, the EU governance deficits noted in this project have led to increases in the cost and time to obtain regulatory approval and political constraints have ensured that even products given a positive scientific opinion by the EFSA are not able to be introduced into European cropping systems. Instead of being adaptive, the regulatory system has become increasingly inflexible and difficult to modify in ways that are appropriate, given the current state of knowledge about the risks and benefits of GM crops.

Innogen has carried out a comparative analysis of industry R&D decision making in the context of pesticide regulatory systems (Chataway *et al.*, 2006).

- We demonstrated that the US Food Quality Protection Act (FQPA), 1996, was *enabling* of innovation by offering incentives for development of products with desirable properties (access to a regulatory fast track) and by *discriminating* among products on an appropriate basis (toxicity to people and the environment).
- The EU Drinking Water Directive (DWD) (80/778/EEC) on the other hand *constrained* innovation by creating disincentives for undesirable behaviour (banning any pesticide that was found to be present in drinking water at a level greater than 0.1ppm) and thereby discriminating among products on an *inappropriate* basis (mobility in soils).

In this earlier research project, the key example demonstrating this difference was the strobilurin fungicides developed by Zeneca Plant Sciences (one of Syngenta's predecessors, along with Novartis). These fungicides are extremely safe to people and the environment and were the first product to be fast-tracked under the FQPA, but were considered by the company to be potentially vulnerable under the DWD. GM crops in the EU today can be regarded as subject to constraining and indiscriminate regulation (see Table 1).

⁴ Innovations are categorised, on the one hand as incremental or path dependent; on the other hand as disruptive or path breaking. The terms 'path-dependent' and 'incremental' are used here to describe innovations that present few developmental challenges to the prevailing system of innovation and are easily accommodated within it. Disruptive innovation steps outside existing paradigms leading to discontinuities in innovation pathways, to major shifts in product types and their place in the market, and potentially to the creation of new industry sectors or radical re-structuring of existing sectors.

Innogen research has identified a set of guidelines for downstream regulation of innovative technologies based on a comparative analysis of industry R&D decision making in the context of pesticide regulatory systems (Chataway *et al.*, 2006):

1. Policy makers should recognise their role in enabling or constraining innovation and take this into account in their decisions - enabling, discriminating regulation works better and faster than regulation that is constraining and indiscriminate in its focus.
2. Where a product has strong potential societal benefits, regulators could consider using policy incentives, such as market mechanisms, infrastructure investment or regulatory fast tracks, to speed up the regulatory process and create a selective advantage relative to other products.
3. Regulatory decisions should balance both risks and opportunities to people and the environment, rather than focusing exclusively on risks.
4. Policy makers should be explicit about political influences on their decisions.
5. Regulatory science should be an important component of the process of adaptation, considering technical solutions as alternatives or complements to conventional regulation.

Table 1. What works in regulatory policy

Enabling regulation (carrots rather than sticks)	Provides encouragement or inducements to undertake a desired course of action Affects the <i>speed</i> with which a particular regulatory policy is able to exert its influence
Discriminating regulation (akin to Nudge Theory)	Discriminates among products on an appropriate basis to favour those that deliver the desired policy aim The extent and appropriateness of its discrimination among products or processes will determine a policy's <i>effectiveness</i> in guiding product development in particular directions
Constraining regulation	Creates disincentives to undertaking undesirable actions
Indiscriminate regulation	Regulates all products in a class similarly and on an inappropriate basis, regardless of their properties

6. A More Balanced and Constructive Approach to Stakeholder Engagement (CSE)

Life science innovation has been at the forefront in the development of public and stakeholder engagement as part of the new governance agenda for science and technology. As one response to the governance deficit in the development of GM crops in Europe, the opportunities for members of the public and pressure groups representing them to engage in dialogue about the development of new technologies, and through this to influence policy, has increased dramatically, and formal public dialogue has been undertaken much further upstream in the innovation process. While the aims of the engagement agenda on GM crops are laudable, the process itself has not been without problems, including undue optimism about our capacity to foresight technology developments and societal needs on a timescale of more than five years, the malleability of public opinion, and the vulnerability of stakeholder engagement initiatives to

manipulation by vested interests (Tait, 2009a). Innogen's guidelines for constructive stakeholder engagement have been developed in order to address some of these issues.

We make a distinction between 'engagement' and 'dialogue', the former implying an intention to take action based on preferences expressed in the discussion, and the latter implying a process of mutual information and exchange of ideas and perspectives with no expectation that specific actions will arise from the discussions.

6.1 Upstream engagement/dialogue

Dialogue at the upstream stage should involve a wide spectrum of societal interests and values, and consider the nature of the research processes involved and the expected outcomes of this process, in terms of product types and their expected risks and opportunities. Ideally, it should be a process of dialogue and explanation where those with different areas of expertise and different interests and values explain their perspectives in an open ended manner. However, to date, most upstream engagement initiatives have involved a relatively narrow spectrum of interests, values and expertise with a strong emphasis on members of the general public and NGOs as their representatives, often accompanied by the presumption that some action will ensue, building on the outcome of an engagement initiative (Stilgoe and Wilsdon, 2009).

Our view is that the focus for discussion at this stage should be mainly on the research process itself. Where this may present specific hazards, it is valid to take account of public concerns and values in deciding whether certain aspects of research should or should not be undertaken and what precautions are needed, e.g. in terms of containment for research on new biotechnologies. There should also be dialogue about the nature of future products arising from the scientific research. However, given the nature of innovation processes and limited human foresighting capacities, it is not appropriate to make decisions at this stage on which types of product should be developed or on how they should be developed. It is certainly unwise to make decisions on funding of basic science based on such engagement activities.

We propose the following guidelines for managing dialogue and engagement in an upstream context with a view to avoiding domination of the engagement process by participants with value-based or ideological commitments:

- Focus on the process of dialogue rather than promising to take action based on the outcomes of engagement.
- Include a balanced range of stakeholders - scientists, company managers, interest groups (e.g. farmers), NGOs and citizens.
- Support individual choice where possible and consider carefully the ethical circumstances where it would be valid to allow the values and interests of one group to restrict the freedom of choice of others.
- In addition to the science and risks of potential new developments, include in the dialogue discussion about innovation and regulatory processes and how these can be used to safeguard against future risks.
- Set standards for the quality and breadth of evidence brought to the discussions and encourage willingness to listen to, and to accommodate, the views of others.
- Encourage a better understanding of science so that people are able to judge for themselves the quality of the evidence presented.

6.2 Downstream engagement/dialogue

Engagement or dialogue in the downstream area should focus more on the technology and innovations in development, rather than the research process that led to them. While the views of the general public are relevant here and should be included, there should be an equally strong focus on those directly affected by, or interested in, the innovative technology being developed, e.g. with farmers, supermarkets and consumer organisations in the case of GM crops.

Engagement in contentious areas like GM crops can increase levels of conflict rather than leading to mutual accommodation (Tait, 2009a; Sunstein, 2009) and this can lead to increased public pressure on policy makers and developers of the technology throughout downstream development of products, making it more difficult to deal with deficits in risk governance. Thus, although the above guidelines for upstream engagement are also broadly relevant at downstream stages of technology development, the focus should be on more concrete applications of the technology, how they are likely to be developed as innovative products, how their risks will be regulated by pre-existing or new regulatory systems, and the societal and economic benefits they may deliver.

7. Conclusions and Discussion

7.1 European Governance of GM crops

The European regulatory system for GM crops is widely regarded as a failure of evidence-based risk governance - it is one of the most onerous regulatory systems in existence for commercially traded products, despite a lack of evidence of health or environment-related risks (The Netherlands Commission on Genetic Modification (COGEM), 2006; Nature (Anon), 2007; Morris and Spillane, 2008; Tait, 2008; Masip *et al.*, 2013). Research undertaken for this project has reinforced, and provided additional evidence for, the conclusion that the EU governance system for GM crops is overly dominated by political considerations, despite the claims of EFSA to avoid undermining the scientific evidence base (Devos *et al.*, 2013a).

The identification of a 'policy gap', as outlined in Section 1 above, could lead to the conclusion that the failure of the EU system lies in its pretence that regulation can be based solely on scientific evidence and that, rather than making its political objectives clear, this political influence leads the Commission to obfuscate by requiring more evidence on the basis that reducing scientific uncertainty will lead to better decisions. Collins *et al.* (2010) acknowledge the importance of values and political motivations in influencing regulatory decisions but they also make the case for a clearer separation of scientific evidence and political influences. The theoretical structure of the EU regulatory system whereby EFSA deals with the scientific aspects of product approval and the dossier is then passed to the European Commission for the final decision with an acknowledged political overlay (Section 3) could be seen as an attempt to make this separation, but the two case studies discussed in Section 4 demonstrate the extent to which political influences have also become an integral part of the EFSA role.

Disputes based on normative values will not be resolvable by provision of information based on scientific evidence (Tait, 2001; Devos *et al.*, 2013b) and the role of the social sciences to date in decision making on GM crop development illustrates this point. The focus has been on stakeholder (mainly citizen) engagement as a means of achieving consensus around the development of GM crops. The focus of this academic agenda was very explicitly not to persuade citizens to accept specific innovations, but to guide governments to focus their research and innovative support activities towards areas that European citizens currently favour (Wilsdon and Willis, 2004). This is typical of the kind of research agenda that arises from a narrow focus that is confined within the methods and concerns of a single academic discipline, in this case mainly sociology.

One of the conclusions of this project is that the answer to politicisation of the EU regulatory system cannot lie in clearer definitions of safety and harm. Rather than lack of clearer definitions making it easier to delay decisions, the political desire on the part of some countries to delay decisions will preclude giving clearer operational definitions. Thus, while a focus on the policy gap helps us to understand the problem, that understanding does not give us any leverage to resolve it. This project has broadened the social science perspective to include our understanding of innovation and governance processes (Figure 1) and has demonstrated how the focus on engagement alone is an inadequate basis for decision making on which research to fund and how to promote specific types of innovation arising from that research.

The complexity and intractability of the EU risk governance problem requires a broader, more systemic approach to its resolution and our proposals for a more adaptive approach to the governance of GM technologies in Europe, along with a more constructive approach to stakeholder engagement, could go some way to meeting this challenge. This report makes the case that the currently restricted array of social science inputs to decision making on life science innovation, while it may lead to interesting academic research, is an inadequate basis for decision making about which basic science to fund, which innovations to support, how best to provide that support, and how to govern emerging biotechnologies. As outlined in Sections 5 and 6 above, we need a more adaptive and balanced approach to the governance of new biotechnologies, along with a more constructive approach to stakeholder engagement.

The role of the impartial academic here, as honest broker (Pielke, 2007), is to clarify possible outcomes and seek to expand the choices available to decision makers, but to refrain from advocating any particular course of action. Likewise, the work of Collins (2008) in support of the role of scientifically informed experts in science policy decision making would restrict the role of citizens to political processes where a democratically determined balance of perspectives should be considered. In this spirit, our view is that the recommendations in Sections 5 and 6, mainly actions for government and policy makers, could have a role in tailoring the innovation ecosystem (or external operating environment) to enable scientists and companies to develop GM and related technologies that will meet societal needs in a safe, affordable and indeed profitable manner.

7.2 The Future Governance of New Technologies for Agriculture

New technologies have the potential to lead to agricultural innovations that are path breaking or radical, and others that are path-dependent or incremental (Tait, 2007). Radical, path breaking technologies are more likely to open up major new industry sectors that have the capacity to provide answers for intractable societal problems or to satisfy needs of which we may currently be unaware. Incremental, path-dependent innovations on the other hand will enable important step changes in the efficiency and effectiveness of current innovation value chains, improving the competitiveness of current industry sectors.

For path-dependent technologies there is usually a well defined regulatory precedent that can be adapted to the issues likely to be raised by the new technology. Path-breaking technologies on the other hand present particular challenges for policy makers and risk regulators in that there may be no obvious match between the expected properties of the new technology and an existing regulatory system.

Often a technology can be path-breaking for one industry sector and path dependent for another, and the choice of an inappropriate regulatory precedent can have damaging impacts on the range of innovation opportunities that can be pursued by an industry sector. The agrochemical companies of the 1980s have become the agro-biotechnology companies of today, and looking forward from this point, novel approaches to GM crop development and many aspects of new biotechnologies would now be path-dependent innovations for these companies, given their evolutionary trajectory over the past twenty

five years. For example, Syngenta's Good Growth strategy aims to raise the productivity of major crops without using more land, water and inputs (Terazono, 2013). This approach will enable the company to innovate more effectively and more rapidly using novel biotechnologies than agro-biotechnology companies that retain more traditional product development strategies.

In the context of synthetic biology and other novel technologies, policy makers see the extended programme of upstream engagement that has been undertaken in the UK (Royal Academy of Engineering (RAEng), 2009; BBSRC/EPSRC, 2010) as contributing to avoiding the emergence of entrenched ideological opposition to these technologies. However, it is too early to make this judgement, and there is now a concerted effort by an influential group of NGOs to develop a new wave of proselytising around synthetic biology developments. As was the case with GM crops, the area of maximum policy turbulence, and hence opportunity to influence public opinion and recruit new members to an NGO, is likely to emerge at the transition between upstream and downstream governance in the translation of innovative technology (Figure 2). Many of the new technologies, beyond incremental improvements on first generation GM technology, are not yet close to having a significant market presence, but some developments involving modified micro-organisms are sitting on this threshold, e.g. areas of industrial biotechnology that will enable the bio-manufacture of high value chemicals.

The expected choice in the EU to use GM regulatory systems as the precedent for synthetic biology developments, makes sense in the context of the envisaged areas of application and the expected properties of innovative products and processes. However, in the context of the current nature of the EU regulatory system for GM products, this choice has the potential to create major barriers to future innovations based on synthetic biology and a range of other new biotechnology developments.

The importance of adopting the GM precedent for the governance of synthetic biology in Europe cannot be exaggerated. The existing costs to the EU of the current regulatory system for GM crops, food and feed, in terms of opportunities and jobs lost, companies, industries and countries disadvantaged, and regulatory time and resources wasted, is likely to be multiplied many-fold if this regulatory approach is extended to synthetic biology in its current form.

Achieving an approach that is open, adaptive and supportive of innovation will be needed to deliver the expected public benefits in medicines and healthcare, fine and specialty chemicals, energy, environment, sensors, agriculture and food (UK Synthetic Biology Roadmap Coordination Group, 2012). This will involve understanding, and balancing the interactions among: scientists and innovators; policy makers and regulators; and citizens and stakeholders (Figure 1). Governance decisions will need to be based on a better understanding of how social and technological systems interact and of how regulatory systems can be designed both to maintain safety and efficacy and to guide and support innovation, backed up by better foresighting of societal needs and engagement processes that recognise a broader range of stakeholder perspectives than has been the case to date.

Taking account of these interactions, the development of novel biotechnologies and the delivery of public benefits from the UK investment in basic science will be best served by a governance approach that is adaptive and constructively consultative, as outlined above in Sections 5 and 6. Governance processes will need to be adaptive to different stages in the emergence of novel biotechnologies: in upstream stages of development (Figure 2) the main focus of governance activities will be on the scientific research itself and how it can be managed in the best interests of citizens, companies, the UK environment and the national economy. Any tentative conclusions or decisions about governance of future innovations at this stage should be designed to be adaptive in the face of new and unpredicted innovative outcomes.

Where innovations are moving downstream, governance questions should focus on the nature of the proposed products rather than the processes that contribute to their development, including ensuring adaptive approaches to regulation and constructive citizen engagement. Likewise, at this stage, stakeholder dialogue should focus mainly, but not exclusively, on the innovations themselves and their relative risks and opportunities.

Policy processes should build on the expertise of a broad range of academic disciplines and stakeholders to address practical questions about innovation in new biotechnologies and its governance. In the natural sciences, there is a need to give balanced consideration to the skills and understanding of engineers, biologists and mathematical modellers. This scientific understanding should form the bedrock for an interdisciplinary social science perspective that includes group psychology, risk analysis, politics and policy analysis, management science and innovation analysis, in addition to the sociology and bioethics approaches that have so far dominated social science contributions to policy decision making.

This will enable a more effective approach to guiding the development of these complex new areas of science and innovation, focusing on interactions that can have a key impact on shaping the future industry sectors involved and the range of innovations that arise from new scientific knowledge, including benefits to agriculture, human health, the environment and the economy.

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ANNEX

Engaging with Uncertainty and Risk in Agricultural Biotechnology Regulation: Delivering Safety and Innovation

RESEARCH QUESTIONS, METHODS AND RESULTS

1. RESEARCH QUESTIONS AND METHODS

The project *Engaging with Uncertainty and Risk* focused on assessment of the environmental risks associated with the introduction of GM crops in the European Union. It addressed the following questions, as proposed by Syngenta:

1. What is the origin of the “risk assessment – policy gap” in the regulation of agricultural biotechnology in Europe?
2. What can we learn from analysis of the risk assessment – policy gap to avoid the imposition of disproportionate regulation of products derived from applications of synthetic biology?
3. How may social sciences help Syngenta to innovate and bring new products to market?
4. What collaborative research projects in the social sciences should Syngenta make priorities?

These questions were complemented by the following objectives from Innogen’s proposal to ESRC:

1. To develop a joint analysis with Syngenta of the nature and origins of the risk assessment-policy gap in current policies and regulations relevant to the approval of the products of agricultural biotechnology in Europe;
2. To conduct two policy analysis case studies of GM crop regulation in the EU, herbicide tolerant maize (GA21) and Bt maize (Bt11), to determine whether and how Innogen’s AGIT and CSE approaches can contribute constructively to improving the analysis of, and decision making on, risk regulation for product approval (incorporating Syngenta research question 2);
3. Through this experience, to develop these Innogen approaches as more widely applicable policy analysis methodologies for a range of governance issues in agriculture-related life sciences;
4. Based on the two case study policy analyses to demonstrate how the ‘risk assessment policy gap’ could be avoided or minimised in the regulation of future agricultural biotechnologies such as synthetic biology, and to make recommendations on how firms operating in this area can engage with policymakers and civic stakeholders to deliver innovative products safely and ethically (incorporating Syngenta research questions 3 and 4);
5. To organise working group meetings to engage with industry, policy makers and stakeholder groups to discuss our findings and methodology and the implications of our results; and to publish Innogen policy briefs and one or more peer-reviewed journal articles, along with working papers and conference papers

The research was conducted in three phases:

Phase 1

To deliver on Syngenta Research Question 1 and Innogen Objective 1, in Phase 1 we explored the origins and impact of the risk assessment-policy gap as perceived by Syngenta and, building on this, developed the Phase 2 research approach. This background scoping phase also included an analysis of the current regulatory approaches for GM crops in operation in the EU, Canada and USA (Section 2 of this Annex).

Phase 2

To cover Syngenta Research Question 2 and Innogen Objectives 2 and 3, Phase 2 analysed the two case studies (GA21 and Bt11) and produced two case study reports

(Section 3 of this Annex). The case studies were based on documentary analysis of Syngenta files related to EU regulatory review of these two products, supplemented by interviews with Syngenta staff in the UK and Brussels.

Phase 3

To cover Syngenta Research Questions 3 and 4, and Innogen Objectives 4 and 5, the outcomes of Phases 1 and 2 research contributed to further discussions with Syngenta staff, and industry, policy and NGO stakeholders. We were unable to organise the proposed workshops in the available timescale but instead conducted telephone interviews with key payers in these constituencies, with a view to informing the organisation of workshops in late 2013/early 2014, funded by the University of Edinburgh.

2. GM CROP REGULATORY APPROACHES IN THE EU, CANADA AND USA

2.1 Regulatory Framework for GMOs in Europe

2.1.1 Summary of Regulations

The main legislative instruments are (Kuiper and Davies, 2010):

1. Directive 90/219/EEC on the contained use of genetically modified micro-organisms (GMMs) dealing with both research, and industrial development.

2. Directive 90/220/EEC was responsible for regulating the environmental release of GMOs until 2001 when it was replaced by the more precautionary **Directive 2001/18/EC**. This directive regulates the release of GMOs into the environment for experimental purposes and the placing on the market of GMOs (for the purposes of cultivation, import or transformation of GMOs into industrial products). This second directive contained a number of important new elements:

- Defined principles for environmental risk assessment;
- Mandatory post-marketing monitoring requirements;
- Mandatory information to the public;
- Requirement for member states to ensure labelling and traceability at all stages whether or not the final product contains modified DNA or proteins (a process-based approach);
- Provision of information for identification and detection of GMOs;
- Approvals for release of GMOs to be limited to 10 years;
- Obligatory consultation with the Scientific Committee of EFSA;
- Consultation with the European Parliament on decisions to authorise GMOs;
- Possibility for Council of Ministers to adopt or reject a commission proposal for authorisation of a GMO by qualified majority.

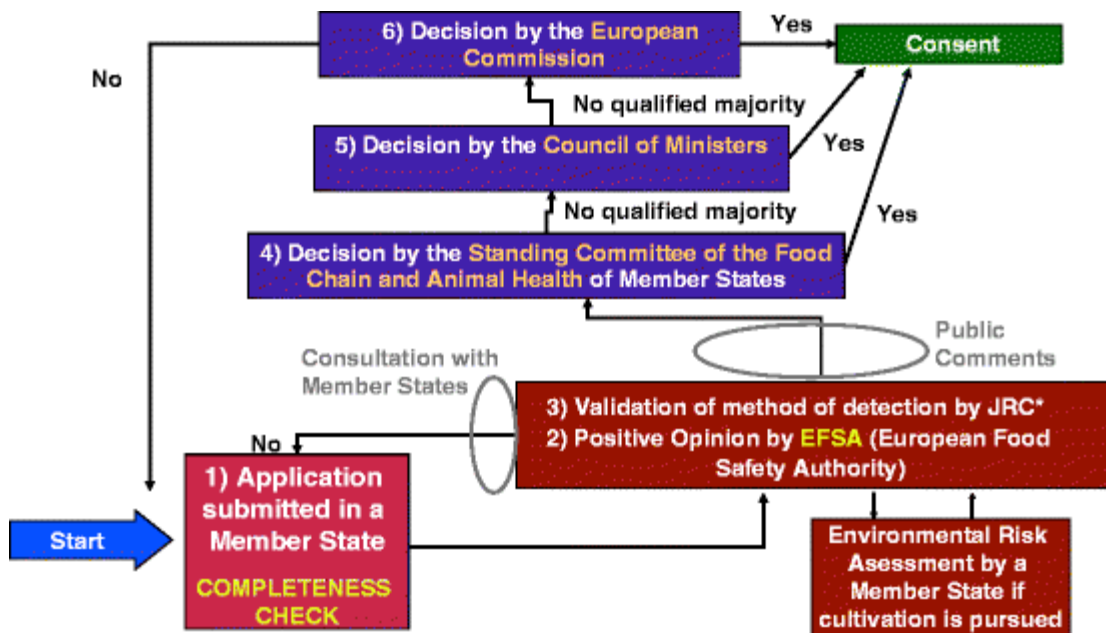
Gomez-Galera et al (2012) have criticised some of these requirements on the grounds that they significantly extend the precautionary approach and make it increasingly difficult to commercialise GM products.

3. Regulation EC 1829/2003 on genetically modified food and feed, which regulates the placing on the market of any GM food or feed, or food containing GMOs.

4. There are two regulatory routes for applicants to submit an application for a GMO: (i) under **Regulation EC 1829/2003** through the “one door one key” principle to obtain authorisation for deliberate release of a GMO into the environment, in accordance with **Directive 2001/18/EC**, and to use this in GM food or feed, in compliance with **Regulation EC 1829/2003**; or (ii) the application, or part of it, may be submitted separately under **Regulation EC 1829/2003** and **Directive 2001/18/EC**. The former provides a more centralised and supposedly transparent procedure (Figure 1).

5. Regulation EC 1830/2003 together with **Regulation EC 1829/2003** prescribes specific labelling and traceability conditions.

Figure 1 Centralised approval system in the EU for GM food and feed (may include cultivation) according to EC Regulation 1829/2003



Source: cited in Costa & Novilla (2012)

2.1.2 Guidance on environmental risk assessment (ERA) of GM Plants

In 2010, the European Food Safety Authority (EFSA) published its scientific opinion and guidance on risk assessment processes for GMOs, in line with the framework of Regulation **EC 1829/2003** and **Directive 2001/18/EC** (EFSA, 2010). This outlined requirements for assessing the potential effects of GM plants on the environment and attempted to provide a rationale for specific data requirements. It stated that the ERA should be 'carried out on a case-by-case basis, following a step-by-step assessment approach.' The document does not address traceability, labelling or co-existence issues socio-economic and ethical issues, being focused on the science and evidence base. It also does not consider the overall risk/benefit or deliberate release of GMOs into the environment for experimental purposes.

The report outlines six steps for the ERA, as indicated in **Directive 2001/18/EC**.

- Problem formulation, which includes hazard identification
- Hazard characterisation
- Exposure characterization
- Risk characterisation
- Risk management strategies
- Overall risk evaluation

The EFSA Scientific Panel on GMOs has seven areas of concern that must be addressed by both applicants and risk assessors:

- Persistence and invasiveness of the GM plant, including plant-to-plant gene transfer

- Plant-to-micro-organism gene transfer
- Interaction of GM plant with target organisms
- Interaction of GM plant with non-target organisms, including criteria for selection of appropriate species.
- Impact of cultivation, management and harvesting techniques
- Effect on biogeochemical processes
- Effects on human and animal health

The starting point for the process is 'comparative safety assessment', the ERA baseline being a conventional non-GM crop (Garcia-Alonso, 2011; Schauzu, 2012). The implication here is that the conventionally grown crop is safe, hence its use as the baseline, and the GM crop must be assessed against this. The comparative assessment is expected to identify differences between the GM and non-GM crop that could potentially lead to adverse environmental effects. Of course, differences will always depend on the nature of the trait. The ERA must be carried out in a 'scientifically sound manner based on available scientific and technical data and on a common methodology for the identification, gathering and interpretation of the relevant data' (EFSA, 2010: p 3).

The outcome of the risk evaluation process should be qualitative and, if possible, quantitative advice to risk managers, 'outlining the nature and magnitude of uncertainties associated with the identified risks' (EFSA, p 3). ERA should follow a 'weight of evidence approach' and consider both intended and unintended effects. The case-by-case approach will mean that the required information may vary depending on the type of GM plant, its traits and the intended use and potential receiving environment.

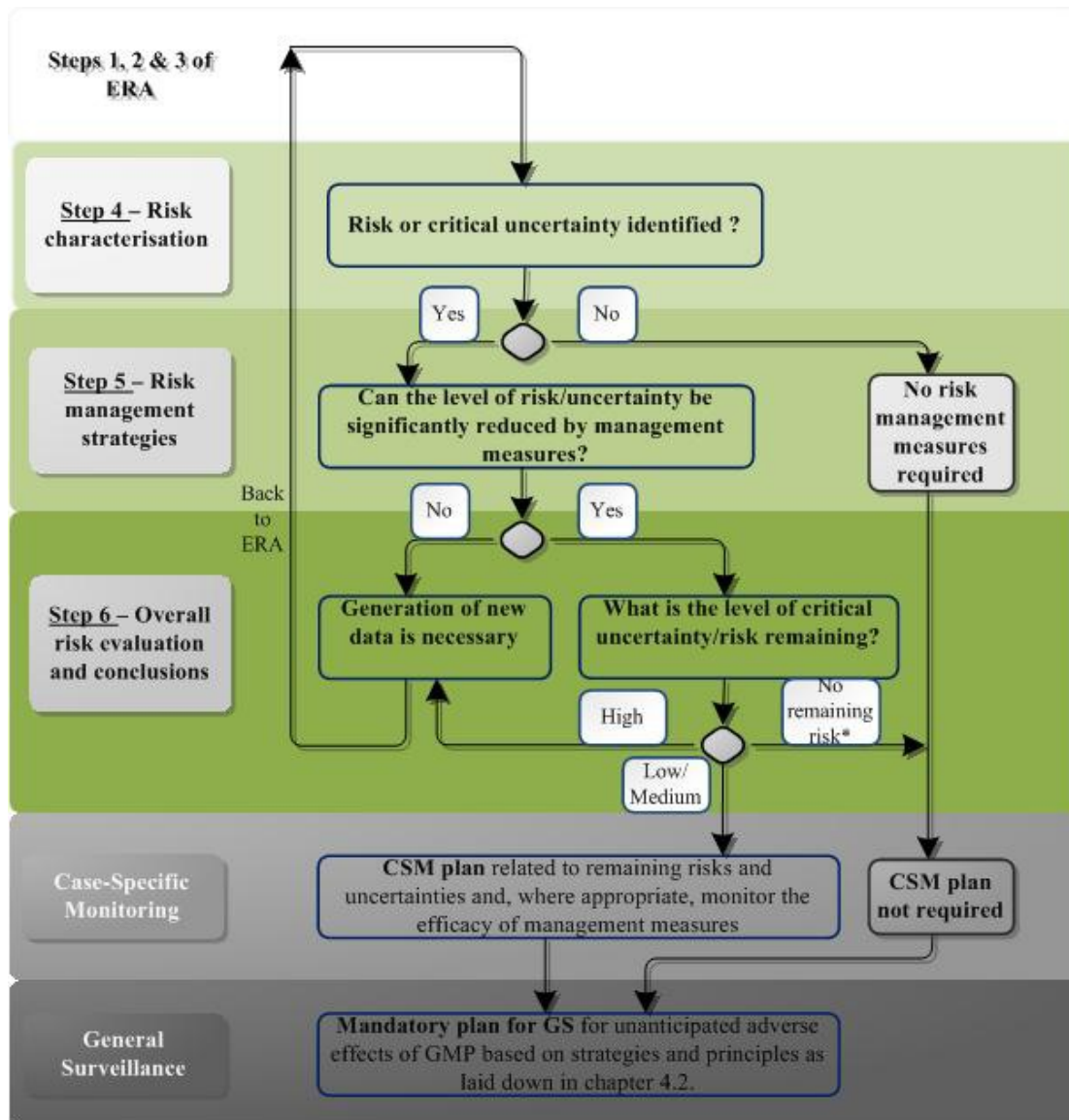
Data and information may be derived from field trial data, molecular characterisation data, compositional data, ecotoxicological testing, modelling and/or desk and literature studies. Interpretation of this data must always be considered in a broader environmental context according to the EFSA.

2.1.3 Post-Market Environmental Monitoring (PMEM)

Regulation EC 1829/2003 requires applicants to implement, if appropriate, a GMO monitoring plan for environmental monitoring in order to place on the market a GMO or food/feed containing or consisting of GMOs. The extent of the market release is relevant, so the plan is targeted rather than considering every possible environmental impact.

A distinction is made between **Case Specific Monitoring (CSM)** (to monitor potential adverse effects of the GMO or its use that have been explicitly identified in the ERA) and **General Surveillance (GS)** (to anticipate unintended adverse events of the GMO or its use on human and animal health or the environment) (Figure 2). GS is implemented if no risk has been identified in the ERA. 'The EFSA GMO Panel is of the opinion that general surveillance is a general overseeing of the geographical regions where GM plants are grown without having any specific hypothesis on adverse effects on human health or the environment. As general surveillance is not hypothesis-driven, it is not conducted using directed experimental approaches.' (EFSA, 87). The EFSA states that existing surveillance systems should be used, if appropriate.

Figure 2: Representation of Steps 4-6 of ERA



*CSM may be required in order to monitor the efficiency of risk management measures (see chapter 4.1.1)

Source, Slides from EC Hearing on PMEM of GM Crops, Brussels, 29 March 2012

2.1.4 Concerns Related to EFSA's Guidance Document

The European Commission intends to include EFSA's guidance document in its forthcoming legislation. Garcia-Alonso (Estel Consult Ltd) (2011) has identified a number of key issues with this document: (i) it is too open to interpretation and difficult to establish the precise data requirements to complete the assessment; (ii) not all of the requirements have a clear scientific justification; (iii) some requirements are difficult or impossible to fulfil given the current status of knowledge (e.g. the long-term environmental effects); and (iv) 'environmental harm' is not clearly defined, so applicants must determine what differences between the GM and non-GM plant might lead to harm, with no guarantee that EFSA will agree with them.

Garcia-Alonso also claims that the document has been opposed by some Member States, due to confusion about what assessment they will need to perform. Applicants have also

opposed it because of confusion over the key data requirements to ensure a complete dossier. On the other hand, NGOs have criticised the document because they do not believe it is sufficiently conservative and precautionary. Thus, a document that was intended to provide a clear scientific and evidence-based template for regulatory assessment has appeared to provide a relatively vague and ambiguous set of protocols that is open to varying interpretations.

2.1.5 Industry Perspectives on the Regulatory Framework and the Market

Since the development of the first GM crop in 1984 the number of new crop varieties containing biotechnology-derived traits has increased significantly. The majority of commercial releases have been field crops such as canola, soybean, maize and cotton, modified to exhibit herbicide tolerance and/or insect resistance (Seed Insight, 2011).

A study by Phillips McDougall (Phillips McDougall, 2011) on behalf of Crop Life International estimated that regulatory science related to development of a new GM variety was \$17.9m (13.1% of total R&D), and registration and regulatory affairs \$17.2m (12.6% of total R&D). The study also found that regulatory science, registration and regulatory affairs accounted for 36.7% of cumulative time involved in development.

EuropaBio (2012) published a table showing timelines for registration of GM products with a positive EFSA safety opinion awaiting Commission action in February 2012, which further highlights the very long delays being experienced by developers of the technology. Some of these delays and product decisions, according to EuropaBio, are not compliant with EU law.

Costa & Novillo (2012), who work for Monsanto in Spain, have argued that the regulatory complexity in Europe, and continued uncertainty, threaten to overwhelm any benefits of the technology, in particular the additional requirements of traceability, labelling, coexistence, socio-economic issues and liability. They state that so far there have been only 6 commercial cultivation approvals for biotechnology crops within the EU, including two Romanian approvals for Roundup Ready soybeans that were discontinued when Romania entered the EU, as opposed to 113 in North America. For GM plants resistant to insects the authors point out that there have been 15 years of widespread cultivation around the world and the number of GM approvals worldwide in 2008 had reached 21 for insect resistance and 5 for virus resistance. It is surprising, according to the authors, that only one product (MON 810) was approved for EU cultivation at that time, although it was later banned in Germany, as discussed below. Two similar insect resistant maize crops have been given positive opinions by EFSA but are not currently being cultivated. Thus, factors other than safety seem to be bearing on the approval process; one being the precautionary principle. The complexity of ERA, local bans and cumbersome coexistence rules mean that European farmers continue to have limited access to GM crops.

Costa and Novillo also argue that changes in genotype may not be larger in a GM crop than in one bred by conventional means, and they question some of the basic assumptions by regulatory bodies about changes within agro-ecosystems. On the broader impacts of labelling, traceability and segregation requirements, they argue that this merely serves to increase the cost of foods and, along with coexistence requirements, is not related to safety.

Industry is therefore concerned that non-scientific and non-risk based issues are driving decision-making about product approvals for GM crops.

2.1.6 Other Issues/Concerns Relevant to Science and Policy

Gomez-Galera et al (2012) also raise concerns about the recent changes in the regulatory framework for GMOs:

- Authorisation for field cultivation of a transgenic crop for research purposes (defined as 'deliberate release' of a GMO by the EU) begins when the applicant submits part B of Directive 2001/18/EC, including an ERA. Although the regulation covers the EU as a whole, the notification must be submitted to one competent national authority (CA) and the power to approve or reject rests with this authority alone. Thus the authorisation of experimental release differs from commercial release under Directive 2001/18/EC Part C, which is determined at the European Community level. The latter involves an EFSA initial evaluation followed by consideration by the EU Standing Committee on the Food Chain and Animal Health. If there is no qualifying majority, a further vote must be taken by the Council of Ministers. The authors state: 'Directive 2001/18/EC requires an initial risk evaluation by the member state where the submission was originally placed but, because objections from other member states are almost guaranteed, EFSA often carries out the evaluation again. Therefore, most applicants now use Regulation 1829/2003/EC (GM food and feed)' (Gomez-Galera et al, 2012: 512).
- A decision taken at the Community level by the Standing Committee and the Council of Ministers is considered final, but they have only reached a qualified majority in one case, leaving the Commission to make the final decision in all other cases. The authors state: 'Even so, individual member states often flout this procedure and *illegally* ban the deployment of approved transgenic crops by misapplying the 'safeguard clause' that allows member states to opt out if they provide compelling new scientific information that offers evidence of risk to health or the environment' (Ibid. p 512). This, the authors argue, can lead to arbitrary and scientifically unjustified co-existence legislation that has a negative affect on GM agriculture. On July 5 2011, the European Parliament approved a proposal to allow member states to impede, restrict or ban transgenic crops legally within their borders. The intention was to stop tactical voting designed to achieve EU wide bans, but the authors believe this will have the opposite effect and lead to arbitrary bans that effectively prevent such crops being growing over large areas of the EU.

Gomez-Galera *et al.* have concluded, based on case studies in a number European countries, that 'The present system for GM field trial notifications in the EU is haphazard, unbalanced and overly complex, strongly discouraging investment in the EU's much-touted bioeconomy. Furthermore, the constant challenges to and a modification of the regulatory system ... do nothing to improve consumer confidence' (Ibid, p 521). Likewise, Fagerstrom et al (2012) argue that 'the regulatory policies within the EU are still rigid enough to prevent most GM crops from leaving the confined laboratory setting; should some candidate occasionally overcome the hurdles posed by these policies, the precautionary principle is invoked in order to ensure further delaying in its use in the field.'

Interest groups are largely blamed for these problems but the risks, costs and disadvantages of not growing GM crops receive little attention. Park et al (2011) have estimated that EU regulatory constraint on farm income to be between €443 and €929 million/year. Fagerstrom et al also argue that the approval decision in practice is not scientific as member states often ignore the scientific evidence and impose their own bans, e.g. the insect resistant GM Maize. MON810 was approved for cultivation in 2005 but suspended by the German Federal Office of Consumer Protection and Food Safety in 2009 on the grounds that it was a potential hazard to non-target arthropods. Some have questioned the scientific justification given by Bohn et al (2012) and Gomez-Galera et al (2012) and Fagerstrom et al (2012) believe that the EU's suggestion to allow countries to reject GM crops on socio-economic or ethical grounds, rather than only on the grounds of scientific risk assessment, will in the end be counterproductive.

2.2 Regulation of GM Crops in the USA and Canada

The GM crop regulatory systems in Canada and the United States are both nominally product-based, although the Canadian system seems to be more purely product based in practice than the US system and also more formal. However, both systems are being criticised on the basis of conflicts of interest and vague definitions and rules.

2.2.1 Canadian system

The Canadian governance system is supposed to be based on science alone, with the formal regulatory process being put into place once a cultivar is obtained (before that, it is the breeders responsibility to manage risk). Three main acts govern the regulation of new crops:

1. The Seed Act covering uniformity, stability and uniqueness of the cultivar, as well as environmental safety (gene flow, invasiveness and weediness);
2. Feeds Act and Health of Animals Act which define the safety threshold for animal feed, fertilizers, livestock feeds, and veterinary biologics, including those derived from biotechnology;
3. Food and Drugs Act which defines the safety threshold for human food.

These acts are designed to cover all aspects of risk for a new plant variety. The Canadian Food Inspection Agency (CFIA) is responsible for enforcement of the first three acts, under direction of the Ministry of Agriculture and Agri-Food. Health Canada is responsible for enforcing the Food and Drugs Act and the safety assessments for all new foods and drugs, including those developed using biotechnology. For products not covered under the above laws, Environment Canada has responsibility under the Canadian Environmental Protection Agency.

The regulations are based on science and scientific evidence and focus on the product rather than the process of development. Plants with Novel Traits (PNT) are defined as those that have been modified via genetic engineering or mutagenesis or do not have a history of safe consumption in Canada. However, a plant is not a PNT if it has an rDNA insertion but does *not* demonstrate a new trait; in such a case it would not be subject to regulation.

A 'novel trait' in respect of seed, means a seed that

- a) has been intentionally selected, created or introduced into a distinct, stable population of cultivated seed of the same species through a specific genetic change, and
- b) based on valid scientific rationale, is not substantially equivalent, in terms of its specific use and safety both fro the environment and for human health, to any characteristic of a distinct, stable population of cultivated seed of the same species in Canada, having regard to weediness potential, gene flow, plant pest potential, impact on non-target organisms and impact on biodiversity (Moran et al, 2009; pg. 6; citing the Seeds Regulation, 1996).

The CFIA states that a plant with novel trait “covers products that have not been previously available for sale in Canada, have been substantially modified, or are produced by a new process (National Farmers Union, 2013).

The Seed Act tends to be the first point of regulation and looks to ensure that any new cultivars are of at least equal quality to those in place. PNTs go through a more rigorous regulatory process than others, requiring field trials that usually last 3 years. The CFIA is the primary agency assigned to evaluating PNTs, receiving a dossier of data from the producer of the PNT regarding quality, disease rating data, and performance

comparisons. A committee of the CFIA (one of 21 recommending committees) assesses the data to determine whether the product is novel, and therefore a PNT, or if the values fall within the limits of previous products. The other agencies involved would be Environment Canada and Health Canada.

There are four options for approval of a PNT:

- national approval;
- regional approval (i.e. Western province versus Quebec and Ontario growing region);
- contract registration for varieties that must be segregated from others for safety purposes; and
- interim registration for a fixed duration for approval of the specific variety.

Most new herbicide tolerant varieties are treated as PNTs regardless of whether they were developed using the rDNA process or traditional breeding. They are assessed according to whether the plant can become a weed or be invasive to natural habitats; the potential for gene flow to wild relatives; the potential to become a pest; the potential impact of a plant or its gene products on non-target species; the potential impact on biodiversity. All plants must have full approval for environmental safety, and must obtain both feed and food approval if they are to be used in either of those contexts. The CFIA takes the lead on most of the evaluation process, and Health Canada takes specific steps regarding any plants to be used as either food or with pharmaceutical properties.

The Health Canada guidelines (2006) state that if a novel food is derived from a plant which is being investigated by the CFIA for environmental release or animal feed, Health Canada should be notified because of equivalent environmental assessment requirements. According to these guidelines, “to increase harmonization and reduce unnecessary delays and conflicting decisions, the CFIA and Health Canada have developed a formalized process to coordinate the determination of novelty for new plant varieties or foods and feeds derived from these plants under the regulatory provision of these Acts,” (pg. 14). When a new request is brought forward for an opinion on the novelty of a plant and its feed and food products, the three agencies will review the case in order to analyze the different factors that can influence its status. If a plant is declared a PNT, then its food and feed products are also likely to be seen as novel. It is also possible, however, to declare a plant not novel but still see its food and feed products as novel, or to have a plant declared a PNT but not have its food and feed products seen as novel because of a history of safe use in other environments.

Bottlenecks exist in the process in that, because it is carried out on a case by case basis, the demand for data is not set and producers are never sure what will be demanded from them. Moreover, they see instances of regulatory creep in that more and more data are being demanded because genetic detection techniques are improving – therefore the scientific tools, rather than actual risk exposure, may be driving the demand for data used in reports. The Health Canada Guidelines (2006) also note that post-market monitoring requirements are also decided on a case by case basis – providing a further potential opening for “regulatory creep”.

Other points of criticism relate to the concept of substantial equivalence, used by agencies to determine whether something is a new product or not, judged on a safety basis in comparison with national products and also international products in similar settings. If a GM crop is determined as substantially equivalent then it can pre-empt much of the need for safety and regulatory analysis; in other words, if a plant is determined to be substantially equivalent, then it does *not* have to go through the full battery of safety tests that it would otherwise have to go through if it was deemed completely a Plant with

Novel Traits; it would only have to undergo testing for the specific aspect that was seen as non-equivalent or truly novel. According to the National Farmers' Union (2013) substantial equivalence is defined as "the equivalence of a novel trait within a particular plant species, in terms of its specific use and safety to the environment and human health, to those in that same species that are in use and generally considered safe in Canada, based on valid scientific rationale." In 2001, however, an expert panel critically identified two definitions of substantial equivalence:

(i) A GM organism is "substantially equivalent" if, on the basis of reasoning analogous to that used in the assessment of varieties derived through conventional breeding, it is assumed that no changes have been introduced into the organism other than those directly attributable to the novel gene. If the latter are demonstrated to be harmless, the GM organism is predicted to have no greater adverse impacts upon health or environment than its traditional counterpart. We refer to this interpretation as the *decision threshold* equivalent.

(ii) A GM organism is "substantially equivalent" if rigorous scientific analysis establishes that, despite all changes introduced into the organism as a result of the introduction of novel genes, the organism poses no more risk to health or to the environment than does its conventional counterpart. We refer to this interpretation as the *safety standard* interpretation (Royal Society of Canada, 2001).

The Royal Society stated that while the second definition would be their preferred one, the first definition has tended to be used by committees in determining whether a plan need undergo the full battery of safety testing. Smyth and McHughen (2007) criticised the Royal Society's position, stating that "there is no scientific reason to suppose that plants developed using rDNA are any more risky than plants developed using other technologies; and second, science cannot prove anything is safe," (pg. 218).

Criticisms have also been made of the transparency of the process where the scientific community or members of the public cannot review details of the evaluation process or the data used. The public cannot verify that the information requirements are in fact being met through the regulatory process. The importance of this is emphasized by the potential for conflicts of interest in the organizational structure and operational practices of the CFIA, its goal being to regulate products and also to promote the development of an internationally competitive biotechnology sector. Furthermore, Agriculture Canada invests \$60M in biotech R&D each year, including collaboration with companies conducting field tests under investment-matching initiatives, which if successful means that Agriculture Canada can benefit from some of the royalties resulting from the R&D.

The committee discussions determining whether a plant is seen as a PNT or not may involve lobbying amongst the different stakeholders at the table given that, once a plant is classed as a PNT, the high cost of regulatory checks and tests, including field tests, will restrict the ability of any body other than a large firm to meet the regulatory requirements and market the product. Researchers will thus try to avoid a PNT designation if possible. Having said that, "to date, in Canada, most commercialized genetically engineered plants have been considered to contain novel traits, and therefore have been assessed for safety," (Smyth and McHughe, 2007; pg. 220). The safety assessment following a PNT designation goes through Stage 1 (contained use); Stage 2 (confined research field trials); Stage 3 (Safety Assessments), and the subsequent presentation of a decision document from the CFIA and other agencies.

2.2.2 US regulatory system

The US regulatory system is based on principles originally set by the White House Administrations from the 1980s onward (both parties) which state that policy should be (i) product-based; (ii) presume low risk from genetic modification; and (iii) review GM products under existing federal standards. The US position is thus very different from that

of the EU in that it rejects strict regulation on the grounds that it would not be based on verifiable scientific risk, and proposes that the technology should be allowed to flourish in the absence of proven hazards. However, there is no definition of scientific risk, and agencies are directed to refrain from hypothesizing what this risk may be or “affirmatively searching for safety or environmental concerns”. The National Research Council in 1987 stated that: there is no evidence that unique hazards exist in use of rDNA or movement of genes between unrelated organisms; risks associated with rDNA are same as those of other methods; assessment of risks should be based on the nature of the organism and the environment into which it is introduced, not by the modification methods. Regulation would occur for the organism itself and/or for products derived from the organism. Much of the onus is on the private developer of a new crop to ensure that it is safe, relying on prudence and fear of liability and litigation.

The political and economic motivation behind the governance approach was to promote the industry’s growth and minimise the regulatory burden on the assumption that effective industry and scientific self-regulation could preclude burdensome or inhibitory legislation. In the President’s Council “Report on National Biotechnology Policy” (Bush administration), federal agencies were seen as gatekeepers to the development and use of biotechnology, and in order to avoid inhibiting growth government should presume minimal risk in the absence of contrary evidence.

The agencies responsible for GM regulation are:

- Food and Drug Administration for food, feed, food additives and veterinary drugs; *is it safe to eat?*
- US Department of Agriculture for plant pests, plants, and veterinary biologics; *is it safe to grow?* and
- the Environmental Protection Agency for on microbial/plant pesticides, new uses of existing pesticides, and novel microorganisms; *is it safe for the environment, safe for new use with a companion herbicide?* (Marden, 2003; pg. 739).

The FDA is the main agency involved in GM regulation, charged with ensuring the safety of human food and animal feeds. Under the Federal Food, Drug and Cosmetic Act (FFDCA) the onus is on the manufacturer to ensure that the product is not adulterated or misbranded. If a food contains a ‘novel’ ingredient, then a company must submit a petition for approval which must contain scientific evidence of its safety and show that there is ‘reasonable certainty’ that it is safe. Alternatively, an ingredient can be Generally Recognized As Safe (GRAS), which means the substance must be ‘demonstrated to be generally recognized as safe among the community of scientific experts knowledgeable about such substances’. With a GRAS designation the lengthy food review process can be avoided. As a result, firms must decide whether they wish to submit a novel food petition or try to demonstrate that they are GRAS. FDA policy set in 1992 presumed that most GM products were GRAS, but it was also subject to a voluntary pre-market consultation process to assure the public that safeguards were in place. However, this is different from the FDA’s position on other conventional food ingredients, which is more conservative and does not presume safety even if it was present in the food supply in other countries or in different formats.

The FDA strongly encourages firms to follow its voluntary consultation process in developing a GM food product and recommends including: a description of the applications of the ingredient or uses of the food; information concerning the source and identities of the genetic material; the intended technical effect of the modification on the food; information on any suspected allergenicity; and comparison with the natural variety. The voluntary nature of this process has meant that firms have on occasion refused to volunteer information requested by the FDA and this relatively soft touch position has led

to criticisms. However, it has been supported by the US courts that have deferred to the FDA's expertise in citing what data is necessary to deem something safe for consumption.

The USDA took an initial position which was more precautionary than the FDA, stating that existing regimes *may* not be adequate for GM products and that some GM products *could* be considered plant pests, be subject to the Federal Plant Pest Act (FPPA), and therefore have to pass through a 'mandatory pre-release permitting process'. The trigger in this case would be the *process* of genetic modification, although the USDA argues that it only applies to those plants that could be reasonably expected to be plant pests.

Criteria used to determine exemption from the more onerous process under the FPPA include:

- the plant is corn, cotton, potato, soybean, tobacco or tomato;
- genetic material is integrated in a stable manner;
- the function of the genetic material is known and does not result in plant disease;
- genetic material does not encode infectious or pharmaceutical substances;
- genetic material does not pose plant virus-related risks; and
- genetic material is not from a known animal or human pathogen.

The producers must inform the USDA that the GM product meets the above criteria, compiling significant dossiers to do so, leading to Environmental Assessments and Environmental Impact Statements, which can then lead to deregulation. The USDA have allowed these criteria for any plant (not just those named) and expected that most GM plant products would be able to meet those criteria. In addition, the USDA introduced a clause that any closely related plants to a GM plant already accepted as non-regulated, would also be allowed through; however, 'closely related' was not defined.

Like the Canadian system the USDA shows some conflicts of interest because the USDA's Agriculture Research Service and Agricultural Marketing Service are also involved in developing and marketing internationally US GM products. The Clinton administration acknowledged this conflict of interest but with the change in administration no action resulted.

The Environmental Protection Agency (**EPA**) **considers** new plants and whether they produce a pesticide. GM products would be investigated based on their production of such pesticides. The EPA's authority would only **prevail where the product has** pesticidal properties; otherwise the USDA or FDA would be in charge. The EPA would use existing regulatory structures to assess new products, **based on** changes in plants that are *intended* to give them pesticidal properties, **and** EPA approval is temporary, **requiring** re-registration at **specified** intervals. EPA approval does not remove the need for USDA de-regulation. Moreover, many of the EPA's permits and registration of products are dependent on their being clear contract obligations between the firms and the potential users of the new plant in terms of how they should be planted and controlled within the environment.

3 GM CROP CASE STUDIES – BT11 AND GA21`

3.1 Introduction

In this case study report, we provide a description and analysis of the risk-assessment process and regulatory decisions that were made in Europe regarding Syngenta's applications to cultivate Bt11 maize and GA21 maize. It offers insights into the risk assessment – policy gap (absence of clear policy/regulatory objectives such that risk assessors have little or no ability to derive robust assessment endpoints) and consider how this has reduced the effectiveness of decision-making processes. These case studies explore the relationship between changes in scientific uncertainty and subsequent policy decisions, and illustrate how scientific risk-assessment and the formal regulatory process (which in the case of Bt11 has evolved and changed substantially since the original application for cultivation was submitted), has not been sufficient to reach a final decision, as the broader political environment for GMOs in Europe has stalled the approval process for the product.

In Section 3.2, we describe the Bt11 product and provide a history of the regulatory process and identify some of the key issues relevant to the risk assessment – policy gap. As will be shown, the Bt11 case study is unique when compared to other GMOs in terms of the approval process. In particular, the initial application submission predated the existence of EFSA, so the product has been subject to a number of different regulatory regimes and has had to adapt to the emergence of new regulatory guidelines and protocols. Furthermore, Bt11 is similar to other Bt products which are or have been placed on the market in the EU. Thus a body of supporting data on the history of safe use of such products is available. This case study provides an illustrative example of how scientific risk-assessment can become entangled with broader policy-related concerns.

In section 3.3, we describe the GA21 product; again providing a history of the regulatory process and key issues relevant to the risk-assessment policy gap. This case study highlights two main challenges. First, a lack of parameters as to what constitutes sufficient and necessary data to satisfy reviewers, despite agreed upon methodologies and scientific process. Second, a lack of agreement upon what constitutes sufficient evidence in studies to demonstrate safety and minimize risk, although this also is tied to parameters of data. We see these challenges reflected in the responses and questions posed by EFSA towards Syngenta's application, as well as EFSA's responses to member country inquiries – the EFSA approach seems to reflect a scientific/objective view, but one that is wrestling with the two challenges above. The challenges are also reflected by member state inquiries and the disparities amongst member states in how they go about evaluating the submission.

The case study will also highlight the very long timelines for approval, despite the formal six month limit imposed by EFSA, due to the "clock stopping" when formal questions and requests for information are submitted through EFSA to Syngenta. This raises the question of how member state questions and opinions filter through EFSA to formal question submissions Syngenta must deal with, and how these member state questions may, intentionally or not, play a role in delays.

Section 3.4 reviews the regulatory/policy process and considers the future for cultivation of these particular products within the EU. Data that informed these case studies were derived from published reports, peer-reviewed articles, material provided by Syngenta, and a small number of interviews (7) with key Syngenta personnel and other experts, as well as information that was collected from a two-day on-site visit to Syngenta (Jealott's Hill), which included a number of recorded meetings with Syngenta scientists and regulatory affairs experts.

3.2 The Bt11 Case Study

The genetically modified insect resistant Bt11 maize provides protection against specific Lepidopteran pests, and also contains a gene that provides tolerance to the herbicide glufosinate. In the initial filing to the French authorities in May 1996 (submitted at the time by Sandoz Seeds), which conducted the first scientific assessment (Notification number C/F/96.05.10), the company anticipated that the seed could replace existing varieties of maize in conventional agriculture. At the time it was already approved by the USDA, the US-FDA and the Canadian CFIA. It was approved later that year by the US-EPA, Health Canada and the Japanese authorities. Bt11 field maize was later approved in 1998 for import of food and feed use in the EU under Directive 90/220/EEC.⁵

Two genes are expressed within the Bt11 derived maize lines. A truncated Cry1Ab (Bt toxin) gene (which is similar to that expressed by the MON810 product) produces the Bt protein, which provides tolerance to Lepidopteran insect pests, such as the European corn borer *Ostrinia nubilalis*. The *pat* gene encodes the phosphinothricin-N-acetyltransferase enzyme, which provides tolerance to glufosinate ammonium herbicides. The genes encoding the genetic traits were inserted into the genome of the maize plants and then, through traditional breeding methods, crossed into additional maize lines.

3.2.1. History of the Regulatory Process for Bt11 Cultivation

The original application to cultivate Bt11 was submitted to the French Competent Authority (CA) in 1996 under Directive 90/220/EEC, which at the time regulated any environmental release of GMOs within the EU. In 1998, Syngenta (then Novartis) were requested to re-submit the dossier to the French authorities, because a new French Biosafety Commission had been formed. In 1999, the dossier received a positive opinion from France but, as a result of Member States' objections, the file was transmitted to the Scientific Committee for Plants (one of the predecessors of EFSA). On 30 November 2000, the SCP issued a positive opinion, stating "*The Committee is of the opinion that there is no evidence to indicate that the placing on the market for cultivation purposes of maize line Bt11 and varieties derived from this line by conventional crosses between Bt11 line and maize lines other than genetically modified ones, is likely to cause adverse effects on human health and the environment*". (Scientific Committee on Plants, 2000)

The application should then have been transmitted to the Regulatory Committee for vote, but nothing happened for two years. The EU was in the process of revising its legislation on GMO marketing, and the new Directive 2001/18/EC approved in October 2002 replaced Directive 90/220/EEC. As a consequence, Syngenta had to submit an updated dossier complying with the requirements of the new Directive.

On 27 February 2003, the French Biosafety Commission issued a positive advice regarding the updated dossier, in accordance with the procedure set out under Article 14 of Directive 2001/18/EC. The overall conclusion of the report was that there was no scientific evidence to indicate that the placing on the market of the *Zea mays* L. line Bt11 posed any risk to human and animal health or the environment for the requested cultivation uses. It stated: "*it might be considered that, according to the present knowledge, the placing on the market of Bt11 maize does not present a greater risk to human health or the environment than any other variety of maize. The updated version of the dossier confirms the initial assessment*".

On 7 July 2003, the updated dossier was transmitted to the EU-Commission and to the other Member States, for review. The dossiers were eventually passed over to the newly established EFSA (set up in 2002) for its official scientific opinion on environmental and human health effects of the product, given that a number of member states had

⁵ Notification C/GB/96/M4/1

questioned the original evidence/data presented by Syngenta, which had been approved by the French CA.

Syngenta's updated application document, including the required Environmental Risk Assessment (ERA), provided scientific evidence to suggest there would be no significant and detrimental impact on human/animal health or the environment.

1. In comparisons between Bt11 maize and the unmodified plant, no differences apart from tolerance to Lepidopteran insect pests and glufosinate ammonium herbicide were identified.
2. In terms of mode/rate of reproduction, seed production of the GM maize lines and hybrids were observed during two field trials in France (1994 and 1995) and no difference was found between the GM plants and non-GM controls.
3. Dissemination of maize occurs exclusively through seed, and maize cannot survive without human assistance due to past selection during the crop's evolution. Seed dispersal of individual kernels does not occur naturally because of the structures of the 'ears' of maize. The GM traits that have been introduced have shown no influence on reproductive morphology so no change in seed dissemination should be expected.
4. Survivability – establishment in the natural environment of a maize population is highly unlikely because disseminated maize rarely grows due to competition with other plants, and the modified traits do not fundamentally change this characteristic.
5. Gene transfer – Maize has no wild relatives in the EU and dissemination of the trait by pollen is only possible to other cultivated maize plants. Furthermore, if this occurred, it would only constitute a fraction of the harvest from neighbouring fields. There is no reported evidence that intact gene transfer occurs from a plant species to micro-organisms in the field situation.
6. Human health – food safety of Bt11 was evaluated in the framework of the dossier UK/C/96/M4/1, regarding import and food/feed use of Bt11 as well as for the notification under the EU Novel Food regulation. No harmful effects were identified.
7. Environment – The Cry1Ab protein is highly specific to certain Lepidopteran pests and has no deleterious effects on non-target organisms. The modified maize does not interact with the environment in a way different from non-modified maize, except for tolerance to Lepidopteran pests. A large number of field trials conducted since 1992 with the Bt11 maize and its progeny have revealed no significant difference between the GM and non-GM varieties.

It should be noted at this point that the Bt11 product is perhaps unique, and certainly different to our other case study GA21, in that there has been a lot of independent research on Bt maize relevant both to the safety of food/feed and environmental impact relevant to the ERA. Although there was not a great deal of third-party data in 1996 when the application was first submitted, subsequent data did provide confidence for regulators, although this was not a formal part of the assessment, as the specific details on these external studies are often not published. Also, as the product has been grown in the United States and many other territories, there is an extensive amount of international data related to safety and environmental impact of cultivation. So this is very different, according to the Syngenta representatives we interviewed, from newer products, where there is less extensive data related to cultivation or history of safe use

The French CA, as already noted, accepted the evidence presented by Syngenta and gave a favourable opinion to the European Commission and Member States. At this point, it appeared that there was a high degree of scientific certainty that the Bt11 product was safe and would have no deleterious impact on the environment or human/animal health. However, following the favourable decision by the French authorities, other member

states raised a number of objections/questions about the status of the scientific evidence and many implied that there was uncertainty about the risk evidence.

3.2.2 Objections by Other Member States and EC Response

The CAs of other member states raised a number of objections to the Bt11 product being approved for cultivation and placed on the market, during the 3 month consultation period in 2003. The first period is 60 days, and then once the company had responded there is another 45 days to resolve any questions. If objections remain after the 45 day period, the file is passed to the Scientific Committee, which in 2004 was EFSA. The principal objections (relating predominantly to the ERA) were the potential adverse effects on soil organisms and arthropods, and the long-term effects on the environment of the Bt-toxin, which is contained in the product. The Commission subsequently considered that the following key issues should be addressed:

1. direct and indirect effects of the Cry1Ab toxin on non-target organisms, specifically soil biota, arthropods, butterflies, and other invertebrates;
2. further data on the effects and persistence of Bt toxin in soil;
3. more information on the general surveillance and monitoring of non-target effects;
4. concerns about potential harm to endangered Lepidopteran species and the possible need to protect endangered butterfly species;
5. potentially altered lignin contents and the biodegradability of plant litter as well as long-term persistence of the Cry1Ab protein.

Table 1 below categorises the types of questions/objections by country.

Table 1: Categorisation of questions from other national authorities after the 60 day period in 2003 (Note the EU consisted of 15 Member States (MS) in 2003)

Member Country	Total questions/statements	Reference statement	Negative statement	Request for more data or clarification	Question/request challenging relevance
Austria	5	0	1	3	1
Belgium	10	1	0	0	9
Denmark	3	0	0	3	0
Finland	3	2	0	1	0
Germany	19	5	1	10	3
Ireland	1	0	0	1	0
Italy	14	3	0	7	4
Spain	1	0	0	1	0
Sweden	10	1	0	9	0
Netherlands	3	0	0	3	0
UK	4	1	0	3	0
Total	73	13	2	41	17

3.2.3 EFSA Opinion (2005)

EFSA (2005) published its opinion on Bt11 for cultivation on 20 April, 2005 (it had started its formal evaluation on 18 March 2004, after Syngenta had provided an updated dossier that included information required for the new guidelines). The EFSA GMO panel considered the initial application, additional information provided by Syngenta (which included a full ERA of the *pat* gene in connection with the possible use of the complementary herbicide), and objections, comments and questions submitted by the member states.

The scientific assessment included:

- Examination of the DNA insert in Bt11 maize
- Nature and safety of the newly expressed proteins produced by the transgenic plants with respect to toxicology and allergenicity
- Comparative analysis of agronomic traits and composition
- Safety of the whole product
- Nutritional and environmental assessment, including monitoring plan.

Although the *pat* gene for glufosinate ammonium tolerance was not considered to be commercially relevant in the EU, the EFSA panel believed that you could not rule out the possibility of farmers growing Bt11 maize with this additional application in mind. Therefore, EFSA decided that the ERA and post-marketing environmental monitoring (PMEM) should also consider direct and indirect impacts of the herbicide tolerance trait. Syngenta had to make a clear statement that it was intended purely as a marker gene and that it was not in the scope of the application to use glufosinate on the crop. According to Syngenta, one of the reports they had to submit to EFSA was an evaluation of what the likely impact of illegitimate glufosinate use might be on Bt11. Syngenta had to conduct this assessment, even though it wasn't technically within the scope of the legislation. Sweden was one of the member states that had a particular concern about glufosinate. The European Commission has recently announced restrictions for the use of glufosinate, which will be effective from November 13, 2013. The active ingredient will only be authorised "for band or spot application at rates not exceeding 750 g ai/ha (treated surface) per application, with a maximum of two applications per year."⁶

Another key issue for this product emerged on 23 March, 2005, when information was submitted to EFSA on the inadvertent release in the United States of a non-authorized GM maize line, called Bt10, and its unintended export as Bt11 for research purposes to Spain and France. The GMO Panel immediately sought information from Syngenta to confirm the risk assessment of Bt11 would not be compromised by the unintended presence of Bt10 maize. Syngenta responded that material used in the safety studies was Bt11 and that it was able to identify and confirm from the Syngenta specific material codes the studies to assess the Bt11 safety were indeed conducted with Bt11 maize.

The substantive response of EFSA to Syngenta's application, and member states' objections (focusing on the environmental risk assessment for cultivation and post marketing surveillance), can be summarised as follows:

1. *Unintended effects on plant fitness due to genetic medication*: Maize is highly domesticated and not able to survive in the environment without cultivation, and maize plants are not winter hardy in many areas of Europe. They have lost their ability to release seeds from the cob and they do not occur outside cultivated or disturbed land. EFSA determined that the Bt11 maize has no altered survival, multiplication or dissemination characteristics except in the presence of glufosinate

⁶ See <http://news.agropages.com/News/NewsDetail---9598.htm>

ammonium. The 'likelihood of unintended environmental effects due to the establishment and spread of Bt11 maize will be no different from that of traditionally bred maize' (EFSA, 2005, p. 15).

2. *Potential for Gene Transfer:* In terms of plant to bacteria gene transfer, given the nature and origin of the genes and the lack of selective pressure in the intestinal tract and/or the environment, the likelihood of horizontal gene transfer conferring selective advantages or increased fitness on micro-organisms is limited. It is therefore unlikely that genes from Bt11 maize will become established in the genomes of microorganisms, and if they did, it would not negatively impact on animal or human health or the environment.
3. *Interactions between GM plant and target organisms:* The panel considered the evolution of resistance in target pests as an environmental and agronomic concern. It concluded that large-scale cultivation of Bt11 maize over several years will increase the selection pressure on corn borers, which might result in resistance to the Bt toxin. However, the panel stated this risk was low as under field conditions and several years of cultivation no resistance has so far been reported.
4. *Interactions between GM plant and non-target organisms:* Reduction in prey either by cultivation of Bt maize or by insecticides may negatively affect the food source of certain predators, but the Panel concluded that current knowledge on toxicity and exposure give sufficient scientific evidence that Bt maize poses no risk to predators. Field studies confirmed that predator and parasitoid abundances and biocontrol functions are similar in Bt and non-Bt fields. EFSA also documented that a range of lepidopteran species may be affected by Bt toxins and some may be present in maize fields. However, it concluded that exposure to the toxins is restricted to those consuming the Bt plant or its products and in Europe maize is not a significant food source for endemic Lepidoptera.
5. *Interaction with abiotic environment:* Assumptions had been made that Bt toxin might persist and accumulate in soil during cultivation of Bt maize and that as a result direct and indirect impacts of the toxin or Bt maize (e.g. potential increase of lignin content in combination with a possible delay in decomposition) on non-target organisms and soil function should be considered. The Panel, however, concluded that this would be a low risk.
6. *Impact of cultivation and harvesting techniques:* The panel considered that the presence of the *pat* gene and the use of glufosinate ammonium are not likely to give an increased impact on biodiversity in most situations. Therefore, it concluded that case specific monitoring regarding any consequences due to the application of glufosinate ammonium in combination with the cultivation of Bt maize is not required. However, the panel recommended that observation of general weed abundance and diversity should be included as part of a general surveillance plan.

EFSA concluded that the data and information available at the time for Bt11 maize adequately addressed all of the outstanding questions raised by member states. It reiterated the original conclusion of the French Competent Authority that Bt11 maize will not have an adverse effect on human and animal health or the environment in the context of Syngenta's proposed use. Again, EFSA seemed to accept that the level of scientific uncertainty surrounding Bt11 was low, as were any potential environmental impacts.

Nevertheless, in terms of the Post Marketing Environmental Monitoring (PMEM), a number of further issues and recommendations were raised by Member States, which are summarised below:

1. A detailed monitoring plan is required that includes both general and case-specific monitoring, and a more detailed insect resistance management plan was demanded.
2. The implications of the presence and use of the *pat* gene, in addition to the *cry1Ab* gene, should be considered in the PMEM plan.
3. More information on general surveillance and monitoring of non-target effects was needed.
4. A considerable modification of the case-specific monitoring plan to take into account the additional requirements for the environmental risk assessment is requested.

In response, the EFSA panel considered these additional issues, critically examined the monitoring plan initially submitted by Syngenta, and requested improvements and clarification from Syngenta.

The panel made the following key conclusions:

1. *General aspects of monitoring*: EFSA considered that the environmental monitoring plan submitted by Syngenta complied with the requirements defined in Directive 2001/18/EC, the guidance notes to Annex V11 and the Guidance document provided by EFSA (EFSA, 2004)
2. *Interplay between environmental risk assessment and monitoring*: Since the ERA suggested that the development of resistant corn borer populations could be induced by cultivation of Bt11, case-specific monitoring of resistance development in corn borers is required (Syngenta had indeed provided such a monitoring plan). The panel also considered whether the abundance of non-target Lepidoptera in or close to maize fields should be monitored, but concluded this was not practical or necessary. The ERA identified no risks specifically linked to Bt maize fields, the influence of Bt11 on variability of abundance of Lepidoptera was expected to be minimal compared with other factors - such as general agricultural management, insecticide use on neighbouring fields, weed abundance, climate etc. – and it would be difficult to compare populations of Lepidoptera in conventional maize fields (which may use insecticides) with Bt11 fields. The Panel also agreed with the ERA that no adverse effects on other non-target organisms are anticipated and therefore should not be included in the case-specific monitoring. It also considered the spread of transgenes to be not relevant for environmental monitoring since sexually compatible relatives of maize are not present in the EU. In terms of the risks specific to the *pat* gene, again the Panel agreed with the ERA that there was no identified risk. So case-specific monitoring was required only for monitoring insect resistance.
3. *General Surveillance*: The panel welcomed Syngenta's use of farmer questionnaires in the surveillance process, but suggested some modifications. First, it should allow for both general farm information as well as field-specific information for several fields when more than one field of a specific farmer is included in the monitoring. Second, the questionnaire sent to the farmers for the year(s) after the Bt maize cultivation needs to be adapted for the monitoring of the specific crops (maize or different) that follow the Bt11 maize cultivation.

3.2.4 Summary of EFSA's Conclusions:

Overall, the EFSA GMO panel considered all the scientific evidence and concluded that Bt11 maize would have similar impacts to those of comparable non-GM maize cultivars on the environment. The only adverse effect identified was the possibility of resistance to Cry1Ab protein evolving in corn borers exposed to Bt11 maize following cultivation for some years. However, the panel accepted Syngenta's monitoring plan for this specific risk.

From data provided by Syngenta, the Panel concluded there was no evidence to suggest that Bt10 material was present in the Bt11 maize used for biosafety studies. Therefore, the risk assessment had not been compromised by the presence of Bt10 maize, which was a concern expressed by some Member States and NGOs.

The EFSA GMO panel was of the opinion that there is no evidence to indicate that placing on the market of maize line Bt11 and derived products is likely to cause adverse effects to human or animal health or the environment for its proposed use.

3.2.5 EC Technical Meeting Convened in 2006

Following the publication of EFSA's 2005 opinion, the European Commission convened a technical meeting with national competent authorities on 19 June 2006 to address any remaining objections of Member States in light of EFSA's opinion. Also discussed was an outstanding cultivation application for TC1507 (a DOW product). Most of the outstanding objections expressed related to the potential effects of Bt11 and TC1507 on non-target organisms and in particular Lepidopteran species and to post-market monitoring processes (EFSA, 2008). Certain Member States did not accept EFSA's previous scientific opinions and claimed their concerns were not being adequately addressed. We might speculate here that political objections wrapped up in the language of scientific uncertainty were related to the lack of transparent policy objectives.

The Commission requested that EFSA complement its previous opinions on Bt11 by providing more specific information concerning Lepidoptera referred to in the EFSA Opinion of 19 January. EFSA was also asked to recommend whether more precise risk management measures (such as monitoring plans) including specific scientific research studies on non-target organisms and taking account of geographical regions, should be implemented. EFSA adopted the Annex complementing its opinion on non-target organisms on the 7 November, 2006 (published 21 November 2006). In this Annex (EFSA, 2006), EFSA concluded that the information for Bt11 and TC1507 clearly addresses the objections and questions raised by Member States, and confirmed that Bt11 and TC1507 are unlikely to have adverse effects on the environment or animal/human health.

Reading EFSA's responses, one can sense a degree of frustration that the evidence is being continually questioned and previous opinions undermined. This has been a recurrent issue throughout the approval process for Bt11, and suggests tension between risk-assessment, scientific evidence and politics, as discussed in the final section.

3.2.6 EC Postpones Decision on Approval of Bt11 Based On 11 New Publications and Invocation of the Precautionary Principle (2007)

In 2007, the Commission highlighted areas where it believed there was continuing scientific uncertainty around Bt11 and concluded that in light of the precautionary principle, Bt11 should not be approved for cultivation. It stated:

'...there are still serious indications that the cultivation of Zea mays L. line Bt11 could (i) adversely affect non-target organisms, such as particular species of butterflies, (ii) increase the presence of parasitoids in caterpillars and thus modify the food chains, (iii) generate an uneven concentration of the Bt-toxin on plants of the same locations, (iv) influence the composition of the microbial community and (v) lead to the persistence of Bt-toxin in aquatic environments. As the studies indicate that the spread of these potential effects in the environment would be wide, the concentration of the Bt-toxin uneven, the affected organisms and eco-systems considerably diverse and their potential damage on

*the environment irreversible, it is not possible to establish appropriate management measures which would effectively mitigate the potential damage on the environment.*⁷.

The Commission cited 11 papers that had been published since November 2006, when EFSA published its scientific opinion, that it believed cast doubt on the long-term environmental safety of *Bt* crops (Abbott & Schiermeier, 2007). Stavros Dimas (EC environment commissioner) stated that he planned to reject Syngenta's application due to potential adverse effects on the environment, which clearly undermined EFSA's previous opinions.

In response to this decision, on November 28th, 2007, the European Federation of Biotechnology (EFB) took direct action to oppose what it considered 'unscientific approaches' to GMO regulation by the Commission. Members of EFB handed over an open letter to Stavros Dimas at the EC, responding to the draft decisions to reject two *Bt* maize products, including Bt11 (Hodgson, 2008). The full EFB letter is included in Section 3.4.

In summary, EFB considered that the draft decisions had no scientific basis and seemed to be made without considering the consequences for Europe or the fact that similar maize varieties have been growing in Europe for the past 9 years with high adoption rates with no adverse environmental effects and in coexistence with conventional and organic farming. Furthermore, concerning the scientific studies (11 publications) contained in the draft decisions that claim to demonstrate environmental risks presented by *Bt* maize, EFB claimed that nine out of the eleven publications actually confirmed the environmental safety of *Bt* maize cultivation and in fact did not identify any environmental risk with respect to the cultivation of *Bt* maize in the EU.

3.2.7 Request from EC for a Further Scientific Review and EFSA's Response (2008)

In a letter dated 24 July, 2008, the EC requested that EFSA's GM panel review previous scientific opinions on Bt11 and 1507 in light of the 11 scientific publications cited in the Commission's decision not to approve cultivation, as well as any other relevant studies. The EFSA opinion published in October 2008 (EFSA, 2008) concluded that none of the 11 publications reported new data for maize 1507 and only two reported new data sets for Bt11. For 2 other publications, it was unclear whether the experiments included Bt11 or 1507. The remaining 7 publications dealt either exclusively with data derived from other GM maize, with reviews on originally published literature to conclude the risk assessment of transgenic plants generally, or to discuss environmental aspects of GM herbicide-tolerant plants, so had very little relevance to these cases.

Each publication was then discussed in detail and assessed by EFSA who stated: *'these publications do not provide new information that would change previous environmental risk assessments – including potential long-term effects – conducted on maize Bt11 and 1507 ... Having also considered other recent scientific publications, the GMO panel reaffirms its previous conclusions on the environmental safety of maize Bt11 and 1507, expressed on 19 January, 2005, 20 April 2005 and 7 November 2006.'* (EFSA, 2008, 21)

From our discussions with Syngenta, the company had very little involvement in this process. It's the responsibility of EFSA to report back to the Commission, and in this case, as well as in responding to member state's questions/objections, they did this largely without requesting Syngenta's input.

In 2009, the EC published an updated draft decision on Bt11 (D003698/01). Having examined the Member State objections in light of Directive 2001/18/EC, information submitted in the notification, and the opinion of EFSA (including its opinion on the 11

⁷ Commission Decision, ENV/07/ p 6 see http://www.gmo-compass.org/pdf/regulation/maize/Bt11_maize_draft_decision_cultivation.pdf

published articles), it concluded that there is no evidence to indicate that placing Bt11 on the market would lead to adverse effects on animal/human health or the environment. It is therefore not necessary to establish specific conditions for the intended use with regard to handling the product and protection of particular ecosystems, environments or geographical areas.

3.2.8 Vote by Standing Committee and Current Status of the Bt11 Product

On February 25, 2009 the Standing Committee on the Food Chain and Animal Health of member states voted on the Commission's proposed adoption of Bt11 for cultivation. In the final vote, 6 countries (91 votes) were in favour, 12 countries (127 votes) were against, while 7 countries (95 votes) abstained and two countries (32 votes) did not participate. As no qualified majority (which would require 255 votes) for either decision was achieved, the Council of Ministers would then have to vote on the proposal. However, during this time there was an important change in the Committee process that might produce a further delay in a final decision being made. Instead of the Council of Ministers, there is now an Appeal Committee constituted by high level officials instead of Ministers. While the lower level of the MS representatives might facilitate the practical work of this Committee, therefore speeding up the process, in case of a lack of Qualified Majority (which is the recurrent outcome with the GM products) the EC is not legally forced to issue a decision. Therefore the final approval for cultivation of a GM product might be postponed until the EC decides the appropriate timing.

If the appeal committee rules against the Commission's proposed action, the Commission must abide by this decision. Full rules and explanation of the Appeal Committee process are provided at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32011Q0624%2801%29:EN:NOT>

If the original process, before the creation of the Appeal Committee in 2011, had been followed, and the Council of Ministers had come to the same decision as the Standing Committee, by law the European Commission would have had to authorise the product. But now, if there is no qualified majority in any sense (which many consider the most likely scenario), the Commission is not forced to act. It can wait until it is convenient to respond, thus creating an indefinite delay.

In most cases, according to one of our interviewees, the Commission would like a qualified majority decision, as it probably does not want to be responsible for making the final decision, due to the political nature of the issue. With a small majority of votes in favour, it seems that the Commission does not want to make the decision to approve.

After more than 17 years in the approval process, the Bt11 product is still without a final approval and it is not clear when this will now happen. One continuing stumbling block is the lack of agreement on the Post Marketing Monitoring Plan (PMMP). A few years ago, according to one of our respondents, 3 companies had insect-resistant corn and decided on an agreed monitoring plan for Bt maize, but the Commission rejected this. When DG SANCO took over the file, it recognised the benefit of the plan and decided to work with it, but there is still no agreed PMMP proposal from the Commission. Bt11 could have been approved without this PMMP agreement in the past, but now it is a formal requirement and this is contributing to the delays.

3.2.9 Additional Data/Research Conducted by EFSA and Role of Syngenta throughout the Approval Process

We have outlined the sequential process of approval for Bt11 and identified key areas where risk-assessment has become enmeshed in broader political complexities and uncertainties. In this section we will focus on the regulatory science that was being conducted within EFSA, and Syngenta, throughout this protracted approval process.

In our discussions with Syngenta, it was clear that throughout the 17 years in which Bt11 has been stuck in the approval process, Syngenta has not had to provide a great deal of additional information from in-house studies, and has not had to conduct extensive additional field trials or experiments in response to comments/questions from member states and changes in the science and regulatory process since the emergence of EFSA. One of the reasons for this is that there has been a lot of independent research on Bt maize and its environmental impacts. Also, and perhaps more crucially, Bt11 maize has been cultivated on a large scale in the Americas since 1998. In addition Bt11 is very similar to MON810, so research data on MON810 and other similar events, such as Bt176, does provide evidence to support the safety of Bt11, although as already stated these data have not been used for formal risk assessment. Nevertheless, some of the comments, questions and objections member states had to MON810 would also be applicable to Bt11.

EFSA took primary responsibility for responding to questions, by reviewing the literature, asking Syngenta for information where necessary, and in some cases developing its own risk-assessment methodologies. One example of this was EFSA's development of a new mathematical modelling system in 2010 for MON810, which was developed further in 2011/2012 to simulate potential adverse effects from the exposure of non-target Lepidoptera to maize Bt11 under hypothetical agricultural conditions within the EU, and provide data on factors affecting the efficacy of risk mitigation measures through the insect resistance management plan (EFSA, 2012). The conclusion was that the risks were low, but would need to be considered in the PMEM under certain conditions (sensitivity and occurrence of harm to non-target Lepidoptera, acreage of Bt maize and host plant density etc) to reduce exposure. In the 2012 paper, EFSA suggested the required isolation distances around protected habitats within which sources of maize Bt11 and MON 810 pollen should not be cultivated. General surveillance, it was suggested, should be used to report on any unexpected outcomes.

So what was EFSA's motivation to conduct its own in-house studies? In most cases, EFSA usually stops work once it has completed and published its scientific opinion. One of our interviewees suggested that the reason is partly due to the fact that this Bt11 product has been in the system for so long and been subject to many delays, during which new data and evidence emerged and regulatory systems were modified. So EFSA found itself routinely being asked by the Commission to re-analyse data. The modelling was an in-house initiative of the EFSA GMO panel, as it believed it would be a useful tool and wanted to test it. Now any regulatory system ought to consider new relevant evidence. For example, if a problem is identified in an approved product, it may be sensible to take action to amend or revoke its registration. However, the problem in the case of Bt11 is the continual introduction of evidence that is irrelevant; that is, evidence that does not question the conclusions of previous studies or simply has no plausible relationship to environmental harm. Under the present system, it seems that the act of conducting a study on a product (or something similar), whatever its objectives or conclusions, is itself a reason for delay.

3.2.10 Syngenta Field Trial Applications

Syngenta has submitted many field trial applications since 1996, in different countries within the EU, but most have been conducted in Spain. For example, Syngenta submitted an application to conduct a field trial in one region of Spain (4 sites in Castilla-La Mancha) in 2008. It is a useful example to further illustrate the regulatory challenges. The purpose of the trial was line multiplication and to collect complementary data from Bt11 maize field performance⁸ A similar document was also submitted in 2009, but on that occasion the National Biosafety Commission sent Syngenta a letter requesting additional information

⁸ Notification B/ES/08/29

on the field trial practices. In 2009, Syngenta also requested permission for a field trial of the stacked hybrid maize Bt11 and GA21. Interestingly, the Biosafety Commission used the opportunity to request additional information on the single events. In both cases, Syngenta responded by letter to the questions.

In its letter, the Biosafety Commission stated that it had looked at the notifications B/ES/09/38 and B/ES/09/09, corresponding to field studies with genetically modified maize plant (Bt11 and GA21, respectively). During its meeting, the members of NBC agreed to focus on the following aspects:

First, given that the objective of the field studies is the multiplication of Bt11 and GA21, it is assumed that the majority of plant material obtained will not be destroyed but rather will be gathered as whole ears of corn for later analysis. In this sense, the NBC considers it essential that detailed information be submitted regarding the precautionary methods that will be taken to avoid possible accidental dispersal during transport of said crops and that accidental entry into human or animal consumption, as well as information on the laboratories that will be receiving the plant material. It would be convenient, according to the NBC, to produce a traceability document of GM maize plants so that the receiving laboratory produces a document that corresponds with what it actually receives. The NBC would prepare a document elaborating the methods of managing risk for these types of cultivation field studies.

Second, the design of the field studies should be presented, indicating the location of Bt11 and GA21, non-transgenic varieties, and other possible “events of transformation” from Syngenta on the same parcels of land.

Third, in notification B/ES/09/38, regarding field studies for Bt11, there is no indication that there will be a border of various rows of conventional maize around the field studies; this measure is considered essential to avoid the transferral of genetic material.

In its response to the letter Syngenta claimed that the characterisation and chromosome placements in the product had already been described. Furthermore, in the context of the effects on non-target organisms, Syngenta maintained that this is not an issue, and referred back to EFSA’s 2008 evaluation and review of the latest studies, which supported this view.

This is another example where Syngenta must refer regulatory authorities to earlier studies and previous evaluations to demonstrate that current questions are largely irrelevant or have already been answered.

3.3 The GA21 Case Study

Maize GA21 was developed to be tolerant to the herbicide glyphosate with the introduction of a gene for the modified enzyme 5-enolpyruvylshikimate-3 phosphate synthase (mEPSPS). Glyphosate is phytotoxic to a range of plants by inhibiting the EPSPS protein, which leads to biosynthesis of key amino acids, leading to plant death. The mEPSPS protein is not inhibited by glyphosate and still performs the necessary EPSPS function in maize, thereby rendering the plant resistant to the herbicide.

GA21 will be used for food and feed, and the application to EFSA on 16 July 2008 included permission for import, processing *and* cultivation (it had already been approved for import on March 28 2008 from an application submitted on July 29 2005).

3.3.1 History of the GA21 Application Process

On July 12 2008, EFSA received from the United Kingdom CA the application for authorization of genetically modified GA21 maize made by Syngenta Seeds. The scope of the application was to include cultivation in Europe. The application was made available to

member states by EFSA on 4 August 2008. EFSA also began to evaluate completion of the application. EFSA decided the application was valid as of 21 October 2008 and “started the clock” on the process. From this point, EFSA endeavoured to keep the application process to 6 months, and gave member state competent authorities and risk assessment bodies 3 months after receipt of application to make their opinion known.

From 3 February 2009 to 21 December 2009 (227 working days) EFSA stopped the clock to request additional information. It stopped the clock again on 12 January 2010 to 19 October 2010 (202 working days); and again from 26 October 2010 to 29 November 2011 (286 working days). *The overall time delay or “clock stop” was 715 working days.*

3.3.2 Technical dossier Appendix 28 Environmental Risk Assessment (ERA)

Syngenta submitted an environmental risk assessment, structured according to the Scientific Panel of Genetically Modified Organisms and following the principle of Directive 2001/18/EC. The Appendix submitted by Syngenta lays out the principle they adhere to for risk assessment, which is “tiered assessment” that offers an “efficient and effective” means of assessing risk from GM crops.

The document states that confidence lies in the rigour of hypothesis testing, and further studies should not simply add data but rather add to the rigour of previous studies. Further studies are only required if the rigour of those initially conducted does not satisfactorily provide evidence of low risk. This question of what constitutes rigour in methodology and conclusion framing will be noted as an issue below.

Syngenta’s evidence to determine the potential environmental impact of GA21 is based on comparative testing with non-GM maize and noting the difference. Syngenta assumes that the impact of conventional maize cultivation is considered to be acceptable and that GA21 will be non-harmful because its characteristics closely match non-GM maize. In addition to the comparative assessment, numerous safety studies were performed to illustrate that the expression of the protein is highly unlikely to be toxic or allergenic.

Risk assessment 1: Likelihood of GM crop becoming more persistent

Syngenta presented data about non-GM maize to argue that maize in general is not likely to become persistent in the natural environment, and that deliberate cultivation is needed for its survivability. The structure of domesticated maize makes it difficult to self-germinate and survive, and the introduction of the GA21 event is very unlikely to cause maize to regress to its primitive form (which would be able to germinate and thrive in the natural environment – regression would involve significant changes in the plant). Furthermore, the mEPSPS protein expressed in GA21 containing maize only provides tolerance to glyphosate, which would provide no advantage, except in the presence of glyphosate and therefore should not make it more durable in the wild or areas where glyphosate is not used.

Risk assessment 2: Selective advantage

GA21 has no selective advantage when glyphosate is not used.

Risk assessment 3: Gene transfer to other sexually compatible species

Syngenta states that the only species that might be sexually compatible and hybridize with GA21 are not present in Europe, and likelihood of gene flow to wild relatives is therefore negligible. GA21 can cross-fertilize with other maize, but maize pollen is heavy and therefore 98% of pollen falls within 25-50 metres radius of the source. Considering possible wind variations and other factors, Syngenta has projected that 200 metres is sufficient to maintain 99.9% purity with other maize varieties in the vicinity of a GA21 crop. These figures relate to field trials and the safety margins necessary for these trials. In terms of commercial application, the assumption is made that there will be a degree of cross-pollination due to different risk management practices; this also raises the standard

of safety as regarding the crop itself as any conclusions carry this assumption of cross-pollination.

Risk assessment 4: Target organisms

There are no target organisms. GA21's target is glyphosate rather than an organism that may interact with the crop.

Risk assessment 5: Possible effect on non-target organisms

Syngenta believes that GA21 is unlikely to be different in its effects on non-target organisms from non-GM maize. The Shikimate pathway of EPSPS is not present in animals, and for plants mEPSPS is 99.3% identical to EPSPS which is ubiquitous in plants, therefore toxicity is very unlikely.

Risk assessment 6: Effect on humans

Based on the mEPSPS structure, and the genome pathway, the hypothesis is that GA21 would have little effect on humans beyond a normal maize effect. This was tested for acute toxicity in mice, with no noted effects. This was corroborated by a number of studies.

Risk assessment 7: Delayed effects on animal health?

Again, because of its similarity to non-GM maize, there will likely be little effect. It has also been tested on rats and poultry.

Risk assessment 8: Delayed impacts on environment?

EPSPS is ubiquitous in soil and microbes, the negligible possibility of gene transfer from GM plants to bacteria would still likely not be harmful because of similarity to EPSPS.

Risk assessment 9: Cultivation effects

Using rotation of crops and crop management systems (i.e. herbicide) should be able to control for adverse bio-diversity or troublesome plant effects. Syngenta argues that there would be no real difference from other maize agriculture.

3.3.3 Czech Republic assessment

On 1 August 2008, EFSA requested the Ministry of the Environment of the Czech Republic to carry out the environmental assessment, which the Czech government confirmed on 8 October 2008. EFSA requested the Czech authority to be finished by 4 months after the 21 October date; in the course of reviewing Syngenta's material, the Czech Republic identified in two rounds of review the need for additional information from Syngenta.

On 16 January 2009, the Czech authority formulated a set of questions and requested provision of information from Syngenta. The clock was stopped on 3 February 2009. The requested information mostly revolved around the change in agricultural practices; information relating to the GM plant; potential change in how the plant interacts with the environment resulting from its genetic modification; chemical use and the essential monitoring plan.

Syngenta replied on 14 July 2009; the Czech authority evaluated the new data and decided that further clarification was needed, and requested for the clock to remain stopped. The extra information requested related to information about herbicide use, regarding data from field trials and the method of statistical analysis for comparison from at minimum three European localities regarding cultivation, management and harvesting. This second set raises the question as to what kind of data should have initially been used

to avoid a second request for further data⁹. They also requested farmer questionnaires to be reviewed. The extra information was received from Syngenta on the 27 October 2009.

Data were delivered on field trials from three different regions; the results showed wide variations per locality with the field trials and question arose as to whether the field trials were properly carried out. According to Syngenta the field trials carried out were not designed to answer the question that was specifically being asked by the Czech CA because herbicide registration was not part of the scope of the Biotech dossier and hence herbicide efficacy data should not be required; the Czech CA focused on the effects of the herbicide used in conjunction with GA21. The herbicide, however, falls under different EU regulation, but the Czech CA wanted to get this information from the data, which were not required in GM studies, rather than from the herbicide dossier. The Czech authority did not expect the applicant to be able to provide further information or provide data correcting the field trials to address concerns regarding the herbicide and therefore asked EFSA to restart the clock and began to prepare its report based on the data available (i.e. that they could not exclude the possibility of adverse environmental effects based on field trials). EFSA, however, stopped the clock again on 16 February 2010 and requested more information from Syngenta.

A new set of questions was submitted, and on 21 July 2010 Syngenta delivered an information package that included studies on non-target organisms, field trials, and additional comments on surveillance of crops. The Czech authority deemed this sufficient and on 12 October 2010 restarted the clock, and submitted their final report on 20 October 2010.

The Czech authority's assessment went through the following different points, the numbering used below corresponding to the numbering used by the Czech authority in their submitted report.

6.1. Genetic modification – just a note regarding this, no major contestation

6.2 GM Plant traits – noted that any differences between GM and non-GM fell within normal biological variation. No real biologically significant difference between GA21 and non-GM maize besides increased tolerance to herbicide.

7.1. Persistence or invasiveness – no real difference to non-GM.

7.2 Selective advantage/disadvantage – no real advantage except when glyphosate used

7.3 Potential for gene transfer – extremely low to plants and animals

7.5 Interaction between GM plant to non-target organism – the main impact not from GA21 but from changes in use of herbicide which could affect biodiversity as would be the case in conventional agriculture.

7.6 Health – no effect

7.8 Impact of cultivation – here the Czech authority disagreed with Syngenta stating that there should be management techniques designed for GA21 cultivation because of potential effect of glyphosate use/over-use on biodiversity. It is worth noting that biodiversity is not defined in EU regulation; regulators instead wait to see the results of studies and then determine whether more information can be obtained based on that. This raises the question as to where responsibility lies

⁹ Assessing chemical use as part of the biotech dossier would put a company in a difficult position as this information was not part of the scope of the dossier and would amount to use of field trial data in a manner for which it was not designed. This point also relates to the different approaches taken by the CA and EFSA.

regarding farming practices and the use of an herbicide in conjunction with a crop. It also raises the more fundamental question as to what needs to be assessed as part of the GM-crop registration versus what needs to be assessed as part of the herbicide registration. Does Syngenta bear this responsibility, the individual farmer, or the member states where the practices are carried out?

8.1 Case specific monitoring – because of change in herbicide use, the Czech CA believes it necessary to monitor potential environmental changes which may be immediate or delayed on biodiversity; the CA believes there is a need to focus on weed shifts, development of plant resistance to glyphosate, non-target organisms, and microbial biodiversity. The focus on weed shifts raises the question as to which weed shifts are harmful and which are simply different; these aspects are again not defined and risk assessment studies can simply turn into scientific research into the ecological effects of glyphosate.

8.2 General surveillance – Czech authority believes that it is not clear how monitoring will be carried out integrating the different data sources used.

Overall conclusion of environmental risk

The Czech CA concluded that Syngenta would need to include a greater description of case specific monitoring, improved general monitoring, and to design a user guide for farmers using glyphosate. The position taken by the Czech CA on where responsibility lies regarding farming practices seems to be that, at least to a degree, some of that responsibility lies with Syngenta.

3.3.4 Question Packages submitted to Syngenta

Czech question set 1 (4 questions):

Question 1 is notable because it states that section 9.1 of the Syngenta application is too simplified and general and requests specification of “all possible interaction and factors that may be considered (comparison to teosinte, rodents and birds) and to take also into account spreading of grains by humans”. This statement in the question raises the issues of what exactly is asked for to determine what information should be submitted.

Question 2 is notable because it states that section 9.3 under Syngenta’s discussion on gene transfer, there is no discussion of its effect on animals and requests such information on animals including microbes/bacteria. Interestingly, this is briefly covered (and repeated in the response to the question) in the subsequent section 9.8 of Syngenta’s application. Did the Czech authority miss this?

Questions 3 and 4 begin to raise the two issues that are upheld by EFSA in the final report – a greater degree of detail regarding farming practices and the use of glyphosate in terms of its managed use, and a more detailed/improved description of general surveillance of the GM plant in terms of approach, strategy, method and analysis.

EFSA Question set 1 (6 questions):

The questions put forward to Syngenta directly from EFSA were mostly requests for further data and justification of data. Syngenta’s responses seemed mostly to provide data already gathered from past studies on the particular topic areas. This latter point raises the question of whether this information had already been provided in the package but not read by the authority, or whether the references to these studies were clear enough that the authority could note them; it also raises the question of whether these data should have been provided as part of the package.

Czech question set 2 (2 questions)

Same as above.

EFSA question set 2 (3 questions)

Set of questions requiring more data and more detailed data sets. For example, the first asks for data on all mEPSPS expression, the second asks for a review of all new scientific data since the last EFSA GMO Panel on GA 21 in 2007, and on non-lethal toxicity effects of GA21.

Table 2. Questions from other national authorities (Appendix G of dossier)

Member Country	Total questions/statements	Reference statement	Negative statement	Request for more data/clarification	Question/request challenging relevance
Austria	25	0	2	5	18
Belgium	4	2	0	0	2
Finland	1	0	0	1	0
Germany	31	3	2	8	18
Hungary	2	0	0	2	0
Ireland	2	0	0	2	0
Italy	1	0	0	1	0
Norway	6	1	1	3	1
Spain	2	1	0	0	1
Sweden	4	2	0	0	2
Netherlands	2	0	0	1	1
UK	4	1	0	3	0
Total	84	10	5	26	43

The total number of questions/statements submitted by member states over the “3 month” period was 84. Of those 84 questions/statements: 10 were simply statements referring to other studies or data the member CA thought relevant in its analysis or which it thought Syngenta and/or EFSA should be aware of; 5 were simply negative statements disagreeing with some element of Syngenta’s submission; 26 were questions/or statements requesting more data or clarification, delivered in a neutral tone (i.e. not questioning the relevance of Syngenta’s study, but asking for more information beyond that submitted); 43 directly questioned the relevance or appropriateness of Syngenta’s studies or of its conclusions based on the study descriptions/data submitted.

The overwhelming majority of questions challenged the relevance or appropriateness of Syngenta's studies. As mentioned earlier, Syngenta's approach to putting together its application package is to limit the number of new studies it must carry out by relying on the rigour, relevance and appropriateness of studies already conducted, explaining its conclusions based on this, and only adding further data in areas where relevance or appropriateness might be challenged.

Of further note is that the majority of questions/statements challenging the relevance of studies in the application package come from two member states: Austria and Germany, with 18 of these questions/statements each. Each of these countries have demonstrated a normative opposition to GM crops in the political realm (Levidow 2005). Each of the member state questions *must* be addressed by EFSA agreeing with the utility of the question and passing it on to Syngenta for further data, or addressing the question by either citing other data or studies that answer the question, or explaining why the question is not suitable for further consideration.

It is also interesting to note that all member countries except Germany had only one national competent authority respond to the submission. In Germany, two authorities responded: the Federal Agency for Nature Conservation, and the Federal Office of Consumer Protection and Food Safety (BVL). In two instances, the German agencies disagreed with each other on a specific aspect of the submission. In this case only body (BVL) is the competent authority, the other agency (Nature Conservation) is not.

In the first of these instances of disagreement, the Federal Agency for Nature Conservation stated: "An exposure analysis as well as any experiment addressing the ecotoxicity of GA21 on non-target organisms is missing. Since no data on the ecotoxicity of the whole GMO including the expressed proteins were submitted risks cannot be fully assessed and the dossier does not meet the requirements..." (note, this is responded to directly by EFSA, as described below). The BVL, however, states "The German CA is of the opinion that, in the case of maize event GA21, the assessment of potential risks to non-target organisms can be completed without the performance of first tier tests. The assessment which leads the applicant to the conclusion that effects on non-target organisms arising from the cultivation of GA21 are highly unlikely is *comprehensible and scientifically sound*," (emphasis added).

In the second instance, the Federal Agency for Nature Conservation disagreed with Syngenta's statement that case specific monitoring resulting from GA21 is not necessary, and believes that such case monitoring should cover the occurrence of glyphosate resistant weeds. The BVL, however, states "the applicant concluded there is no need for a case specific monitoring based on the results of the risk assessment. The German CA agrees with this conclusion."

Interestingly, many of EFSA's responses agreed with Syngenta's conclusions, pushing back against member CA challenges, though EFSA does agree in some instances and notes a request made for further data or clarification. An illustrative example of a response from EFSA to the Austrian CA "notes that the approach applied in the comparative analysis is in line with its Guidance Document, which was in place at the time the application was submitted". Also illustrative is a response by EFSA to a question by Germany's Federal Agency for Nature Conservation (see first statement noted above): "testing of non-target organisms without a sound hypothesis would add little to the overall risk assessment." EFSA's responses seem to be split between asking for all the data available within particular areas, mostly in terms of specific studies already conducted, and accepting that previous approval has occurred (therefore a previous study cited was sufficient). EFSA seems to be attempting to remain scientific and objective, but no parameters are set on what is necessary to demonstrate safety. For the most part, EFSA accepts the hypotheses that Syngenta puts forward (i.e. justifying why maize behaves a certain way), but also asks in some instances for *all* data backing the hypotheses.

The most common or strongest concerns were those expressed in the final report – namely the requirement for a clarified monitoring program and a more specified farmer questionnaire. This implies that EFSA to some extent tries to determine the common concern to highlight key changes, but this is not necessarily clear. Also, one might ask if this outcome could have been reached in a faster, more targeted process.

Given that EFSA assigned the environmental review to the Czech Authority, which did not demonstrate hostility to Syngenta's proposal, it is implied that the whole process would have been very different if a different authority had been selected for the environmental assessment, particularly given the above differences in opinion amongst the CAs, including between the German authorities. How does EFSA determine which CA to assign to the task? Are the national authorities given data from previous submissions? How much are national authorities expected to be experts and have access to knowledge of studies on the different areas? There is some indication that this selection is based on willingness and available expertise in the member countries, leaving EFSA with a limited pool of candidates. More information on this from EFSA itself would be useful.

3.4 Discussion and Conclusions

The Bt11 and GA21 case studies highlight the challenges facing industry in getting GMO products approved for cultivation in the EU. They are also illustrative of the widening gaps between risk assessment, scientific evidence and policymaking. Our discussions with Syngenta and review of the literature regarding Bt11 and GA21 specifically, and regulation more generally, revealed a number of key issues.

In both case studies it was clear that the political constraints placed on EFSA have so far made it virtually impossible for their positive scientific opinions about GM crop development in the EU to be followed through in practice. In terms of the general role of EFSA, it often receives reference questions on points it has already answered, but instead of simply stating that the question has been answered, EFSA sometimes feels it is necessary to collect more information and demand additional data. EFSA has always done what is requested of it from the Commission (reanalyse the product, for example, which happened with Bt11), and this always takes time. In the case of GA21, the assessment process split between the more normative "this is not enough data to base your conclusions" or "this is not a rigorous enough study" and the "I understand and agree with this data, however what can you tell us about *this*?" What needs to be determined, therefore, is what are enough data and what are the requirements or criteria for relevance for these studies.

This debate about the nature and meaning of data and requests for clarification or further studies requires a lot of work and causes significant delays in the approval process. One could argue that risk-assessment and regulation should require additional information/ data collection only when there is a clear, legitimate and demonstrable need for it. This perhaps requires a clearer demarcation between risk-assessment and scientific research, as discussed in more detail below.

Second, EFSA and many CA's, as well as a number of NGOs, do not appear to fully recognise the distinction between the science of risk-assessment and scientific research itself. For risk-assessment, a decision can be taken on the basis of a limited amount of research determined by what needs to be known to satisfy regulatory standards, whereas requests for more scientific research in the cases described here often seemed to be generated more in the spirit of open inquiry (nice-to-know). Limiting the data requirement to that needed for a decision also allows for a fixed time line. The initial scientific opinion of EFSA on Bt11 in 2005, for instance, should have represented an endpoint in regulatory decision-making, if risk-assessment was the primary objective. However, since Bt11 has now been in the system for 17 years without a final decision, this has clearly moved beyond a risk-assessment process, according to a number of our interviewees. The same

can be said for GA21. The data that are important to know in order to make an informed decision on the safety/efficacy of these products must be better distinguished from the wealth of data on the products that might be scientifically interesting, but have no direct relevance to risk-assessment. Within Syngenta, only studies that produce data relevant to answering specific questions from regulators are conducted and submitted as part of the regulatory dossier. Furthermore, Syngenta only uses methodologies that are tried and tested (adhere to international protocols, follow GLP standards etc) and where there is some consensus about their validity.

One challenge for EFSA is to establish what the relevant questions to be answered are. One of our interviewees claimed that EFSA often asks companies to go beyond established methodologies to further explore the science, which makes it difficult to assess reliability of results and represents a move away from risk-assessment to scientific curiosity. EFSA published some guidance on risk assessment methodology in 2004, but since then the goalposts have constantly been moving, particularly arising from a mandate from the Commission that unintended, long-term effects should be part of the risk-assessment for cultivation.

Thirdly, the political process appears to be more restrictive than the regulatory process. Regulation can be long and complicated but should, if done correctly, produce an outcome. In the cases of Bt11 and GA21, the political process remains a total barrier to introduction of these products in the EU implying, as described by Syngenta staff, that the problems lie with risk management rather than risk assessment.

Finally, both case study products have already been cultivated in many countries, with no reports of adverse effects. This is important, indicating an absence of harm for both products, but once again raising the question, what constitutes sufficient evidence of safety. Formally, risk assessments test hypotheses that a particular use of a particular product will not cause specified harmful effects. A "negative result" is corroboration of one or more of these hypotheses. The amount of evidence someone requests will be linked to the degree of corroboration they require for the hypothesis of no harm. Some people prefer a single severe test of the hypothesis (a tier 1 study, for example), while others prefer a huge weight of evidence from studies that may only weakly test the hypothesis (if at all). Given that the best we can achieve is corroboration, not proof, of the hypothesis a case can always be made for further testing. This implies that GM applications face (i) a set of normative positions attempting to block the process of approval, and (ii) a lack of parameters specifying what are sufficient data and what issues should be placed on the table, thereby potentially extending the process indefinitely.

Levidow et al (2005), in their study of EU regulation of GM, describe how CAs will assess evidence and either request more information or state that the evidence is sufficient. However, where one CA finds evidence sufficient, many times other CAs raise objections and given such disagreements, including on standards for control measures for use, EFSA has been asked to make its own judgements. In our cases this applies to many of EFSA's responses where decisions can be seen as accepting weak evidence or anomalous results.

The standards for evidence or justification for opposing GM approval are thus not specified and many member state CAs do not provide reasons for withholding support of GM products. EuropaBio, in a short report (3 June, 2013) has noted that "the Commission has formally admitted that it regularly fails to comply with legal timelines when it comes to GM authorizations," (pg. 1). In a March 2013 report, EuropaBio notes that for applications for food/feed/import – not cultivation – the average time for approval for a GM product is 45 months (rather than 6), and 15 months (i.e. one third of the time) is spent after the completion of the EFSA risk assessment. For those applications that include cultivation the wait is far longer. EuropaBio notes that on different occasions EC panel meetings on GM crops have been cancelled. According to how the authorization process is supposed

to work, if EFSA finds an application satisfactory the Commission then votes on whether to approve the product; if a qualified majority of member states is not achieved, a second vote is held. If again a qualified majority is not achieved, the Commission can approve the product (EuropaBio, March 2013); however participants in the process have speculated that, due to the sensitive nature of GM products in Europe, the EC is unwilling to move forward without a qualified majority.

In conclusion, the Bt11 and GA21 case studies illustrate the risk-assessment policy gap, and the continued blurring of the boundaries between risk assessment, scientific research and policy-making. They also illustrate the more general lack of political willingness to approve GM products for cultivation in the EU.

3.5 Letter from EFB to European Commissioner Stavros Dimas¹⁰

Dear Commissioner Dimas,

The European Federation of Biotechnology, EFB, is very concerned to read about your draft decisions to reject two Bt maize product submissions based on discredited scientific arguments that have not been reviewed by your own independent scientific body, the European Food Safety Authority.

We consider that the draft decisions do not have a scientific basis and seem to be made without considering the consequences for Europe or the fact that similar varieties have been growing in Europe for the past 9 years with high adoption rates with no adverse environmental effects and in coexistence with conventional and organic farming.

Concerning the scientific studies contained in your draft decisions, that claim to demonstrate environmental risks presented by Bt maize, nine out of the eleven publications actually confirm the environmental safety of Bt maize cultivation and in fact do not identify any environmental risk with respect to the cultivation of Bt maize in the EU.

Only two of these publications (Hilbeck et al., 2006, & Rosi-Marshall et al., 2007) allege potential environmental risks; the former being a philosophical approach, rather than scientific data, and the latter is a questionable extrapolation from laboratory tests. Indeed the Rosi-Marshall et al. paper is based solely on laboratory experiments, whereas the field data of the same authors demonstrates no Bt effect on aquatic organisms (as shown on their own website). As far as the field test is concerned, it lacks decisive data on which transgenic maize plants were used and the entire experimental documentation appears sloppy and not meriting peer reviewed publication¹. In contrast to the theoretical risk projections of Hilbeck, other authors have published a meta-analysis, of all available studies carried out with Bt crops based on real, scientifically acquired data that confirm there is no indication of ecological risk arising from the cultivation of Bt maize (Marvier et al., 2007; Romeis et al., 2007). There is no new scientific evidence to contradict the conclusions reached by the GMO Panel of the EFSA on the safety of Bt maize cultivation in the EU. Furthermore, in July 2007, the OECD published a consensus document 2 on safety information of transgenic plants expressing Bt.

This document thoroughly reviews and confirms the safety and high degree of specificity of the Bt proteins expressed in Bt maize, including the protein expressed in line 1507.

Another inconsistency of your draft decisions is that they fail to draw on a substantial body of scientific data accumulated over several years and published in the last 12 months that highlight the economic, environmental and consumer benefits of Bt maize. A total of 63 peer-reviewed publications attest to the fact that Bt toxin does not accumulate in the soil and does not affect aerial and soil-based non-target organisms, on the contrary, there is

¹⁰ The documentary references included in this paper are not referenced here.

ample evidence that non-target insects are severely threatened and reduced in their populations by spraying pesticides.

In considering the environmental safety of Bt maize, it is pertinent to note that *Bacillus thuringiensis* has been widely used as an insecticide spray for the control of European corn borer in Europe since 1938, when the first commercial Bt preparation (Sporeine) came onto the market in France. Given that Bt is a commonly used insecticide in organic agriculture and given the current trend in the expansion of organic farming in Europe, and the year-on-year northward spread of European corn borer, it is inevitable that Bt spraying will be on the increase. The scientific data accumulated over recent years as part of biosafety assessment dossiers compiled on the various Bt crop varieties for commercial release will provide useful evidence for assessing the environmental impact of organic farming. As for the present time these environmental assessments of Bt sprays with their much higher concentrations have not been properly carried through, and also not published in peer reviewed journals - this in contrast to the many peer reviewed papers testifying no negative effects in soil and agricultural environment of GM Bt crops.

Agriculture is vital to the European economy, and Europe stands to gain much by the cultivation of new high performance crop varieties. Bt maize ensures productivity in years of heavy infestations and reduces the need for pesticides. In 2006, GM maize varieties including these two products were planted on 25.2 million hectares around the globe, and on 62,187 hectares in Europe. Spain has grown Bt maize for 9 years, and the benefits of Bt maize to Spanish farmers are well documented: average yield benefits have often been 10% and sometimes higher, which adds 15 million Euros income to Spanish growers. Recent field trials in Italy showed that Bt maize performed better than conventional varieties with yield increases of between 28 and 43 percent. These trials demonstrated that Bt maize can not only be more profitable for farmers, but is healthier because of lower contamination with hazardous fungal mycotoxins which represent a significant health threat to humans and animals when present in the food chain (Regulation (EC) No 1881/2006).

Farming systems are very diverse, from conventional to organic or genetically modified (GM). This ensures that agriculture provides an abundant and affordable supply of healthy food and feed, and offers consumers more choice. The EU's explicit policy is that 'No form of Agriculture should be excluded from the Union', and the European Commission asks Member States to develop rules for the coexistence of different production systems, like Bt maize and non-GM maize, all long term scientific coexistence studies on maize demonstrate the feasibility of coexistence. It is important that the consequences of any obstacles to the cultivation of GM maize varieties such as these are carefully evaluated, since a number of alarming indicators point to a future collapse of the EU livestock production due to the unavailability of imported feedstuffs.

The Portuguese Council Presidency has recently called for an open debate on the impact of the EU GM policy on food and feed security, in the light of an extra cost of 2 Bio Euros for EU-livestock producers resulting from de-facto import bans on feed maize and corn gluten feed from GM corn producing countries.

The draft Commission Decisions are totally unacceptable, not only for European farmers and consumers, but also set a terrible example for other parts of the world that presently draft guidelines for the cultivation of GM crops, since they look to Europe as an example. This is especially true in the developing world where there is an urgent need of new technologies to raise agricultural productivity. Other GM strains of maize are under development that will have enhanced nutritional quality or tolerance to drought, and must be given the chance to reach those who need them the most. It is a proven fact that in developing countries Bt maize is healthier due to its much lower content of mycotoxins, which have dramatic detrimental effect on human health (cancer, spina bifidis).

In conclusion, Commissioner, your proposals to not approve the two Bt maize lines for cultivation based on discredited scientific arguments would not only undermine the EU's own scientific advice and risk assessment procedure but would also represent a significant threat to the competitiveness of European farmers.

To impose such bans is economically wrong, and pesticide use for controlling European corn borer would continue, It is also wrong on grounds of human health considerations. European farmers would be denied a valuable economic choice and Europe would import more grain to meet demand, but from where. It would do nothing to support the choice of feed producers or consumers. Such a move would violate EU procedures and without scientific evidence to support them would ultimately be rejected.

As European scientists we urge you to reconsider and return to a reasoning based on science and experience. The consequences of approving these draft Decisions and the precedents they would set would be the marginalisation of science in Europe, the discrediting of the European Food Safety Authority and the collapse of the EU-livestock industry.

Yours sincerely,

Emeritus Professor Marc Van Montagu
President of the European Federation of Biotechnology

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