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Chapter 11.

The Safety Science of Genetically Modified Organisms

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Introduction[1]

Our goal in this chapter is to discover what constitutes the safety model of the GMOs' production. This novel technology represents for safety experts and interested publics a new ball game to experiment whether decades of research in safety management, and safety risk assessment has some value to add to the complex debate shaking the deployment of GMO products since the mid-eighties.

The implicit hypothesis that guided the drafting of this chapter is that yes, there might be some commonalities and mutual benefit to actually envision the GMO controversy over safety with the toolbox of safety science.

Historically the safety science has mostly dealt with high-risk industries (Nuclear Power Industry, Chemical Industry, Aviation Industry) and more recently it has enrolled medicine (See Charles Vincent & Bas De Mol, 2001). It was the objective of the workshop in preparation of this book to further extends the realms of the topics and tackle Genetic Engineering, from a safety management's perspective.

"Classical" Agriculture does not seem to worry the safety experts so much, only when considered through events like explosions of silos, or explosions of batches of fertilizers on sites. On the contrary food safety has always been a concern. The GMO controversy falls into the ever-growing category of food safety related issues. Historians are kindly (and sometimes ironically)

[1] I would like to thank Claudine Burton-Jeangros and Todd La Porte for their important help with this chapter.

warning us against the declared newness of such topics, recalling for example recurrent episodes of worries about the quality of the bread throughout the past centuries (Ferrières, 2002 and Ferrières, 2005; Kaplan, 1996).

Interestingly, Genetic Engineering is the subject of many worries and fears, but is not appearing in the classical literature where safety approaches are discussed. Charles Perrow in his *afterword* for the second edition of *Normal Accidents*, in 1999 (1st ed. 1984) is only mentioning it in passing but does not quote any specific work, for there is no analysis of the "systemic" risks (using Perrow's notion) the GMO industry is posing yet. It is quite remarkable for example that the science of safety mainly developed for industrial contexts has not yet touched upon the daily operations of GMO farms, as if Genetic Engineering, once outside the labs was operator-free, actors-free, as if there was no need to understand and study the current practices of the "first-line actors" (as they are called in other industrial settings) of the system, i.e the farmers[2]. In the context of GMOs, the little we know points towards a model of farmers, knowledgeable but dependant upon the companies that develop and sell the seeds. Therefore, for that reason, this type of farmers looks more like company employees, than independent producers. In this context, the question of their management and the organizational factors of the current agricultural practices are of keen interest to a safety science perspective. This would be certainly an urgent need, as some argue that in the case of GMOs, the large and powerful corporations that are producing the seeds do possess the growing plants, and indirectly the farmers and the fields.

The literature reflects this inclination: It has produced a vast body of studies on expertise and experts in the early days of the inception of genetic engineering. Naturally the "precautionary principle" has been a *morceau de choix* (Godard, 1997; Hermitte, 1997, Bourg, 2001). It has produced capital insights on the intricacies of decision-making in various committees (Roy, 2001) followed by important characterization of the organization of public debates and public acceptance of GMOs (Joly, 2001). One should notice though that such literature is mostly European. Evidently, it has been fuelled by the controversy over GMOs itself in Europe. The differences between Europe and the US have also been a source of interest for scholars notably focusing on the distinctive ways of regulating biotechnological innovations, such as GMOs across the Atlantic (Gaudillière & Joly, 2006). No doubt also that Bruno Latour's passion for scientific controversies has been well teased by the GMOs' battle among others (Latour, 1987, 1999; Callon, Lascoumes & Barthe, 2001). More recently, scholars have also explored the changing characteristics of the food safety

[2] There are some exceptions, when we turn to the economic literature for example. Economists are concerned with choices. Therefore, some papers offer an analysis of the significant variables that affect the adoption of GMOs by specific farmers (Darr & Chern, 2002).

regulation in Europe (Ansell & Vogel, 2006) in the aftermath of Food crisis like BSE or Beef Hormones. Ansell, Maxwell and Sicurelli (2006), for example, tied the GMO controversy to a long list of earlier crisis, which paved the way for a strong and lasting mobilization in Europe. As Ansell puts it: "…the mad cow crisis created an opportunity structure particularly conducive for the mobilization of anti-GMO demands" (p. 335, 2006).
However it stops there. The full-scale development of the technology in many countries requires now a different focus and especially fieldwork studies at the production sites, which would enable us to seriously discuss current agricultural practices, hence related quality and safety practices. These studies are actually missing.
A similar neglect for human and organizational factors issues and risks induced by medical practice was common only 10 years ago in Medicine. *To Err is Human: Building a safer Health System*, in 2000, brought to light a gloomy picture[3] that produced the necessary blow to such a disinterest. The current catching up of the medical field and its dedication to improve the system design of health care are giving us hope that a similar course of action might be taken by the GMO industry.

Plan

In a first section, we would like to compare the GMO industry with the more traditional industries concerned historically by safety paradigms. We will do so by asking whether there is any parallel to be drawn between the GMO industry and for example the Nuclear Industry or the Chemical Industry. A similar attempt had been made by Fahlbruch, Wilpert & Vincent (2001) in their discussion of the transposition of traditional approaches to safety in the field of Medicine. They concluded that Medicine could for example import a lot of the spirit encapsulated in Perrow's theory or in the High Reliability Organizations' proposals. To their view the entry point of the so-called "safety culture" could also be very useful in hospitals. In fact, since the book has been published, some scholars have taken up the challenge and are actually conducting research in hospitals using safety culture surveys and developing experiences based on the so-called HRO principles[4].
In a second section, we will try to unfold the various items, or properties of the implicit safety model of GMOs as they emerged from the chapters of this book and from the lively discussions we had during the workshop. Several concepts have been floated around

[3] The report established, in particular, that more people are dying in the U.S, in a given year, as a result of medical errors, than from motor vehicule accidents (43 458), breast cancer (42 297) or Aids (16 516).
[4] David Gaba pioneered such work (Gaba, 2000, Roberts, Madsen & Van Stralen, 2005; Singer *et Alii*, 2003; Gaba, Singer & Rosen, 2007; Singer *et Alii*, 2007).

and they do contribute to draw a *safety profile* of this industry, even implicitly.
Finally in concluding remarks, we will discuss a couple of « traditional » properties that are at the core of the safety management of high risk industries and see whether they might be transferable to the GMO products and their operating systems. Throughout this journey, it appeared that technological and organizational remediation strategies have not yet been fully laid out. Hence, we will ask ourselves, what could be the institutional and organizational conditions for this production to be successful, and gain widespread acceptance.

1. Parallels that can be drawn

1.1. *A Contested Technology*

One of the first characteristics that strike us is the fact that GMO engineering is a *contested* technology much like the nuclear industry, or the chemical industry, which are also facing fierce opposition, since their early days (Jaspers, 1988 & 1990; Touraine, 1989). Despite the fact that some countries are nowadays using civil nuclear power with little opposition, like France or Japan, the potential of a severe incident would be damaging to the entire industry even in countries, where the public acceptance is high in comparison. Chernobyl has not been the “Big one” (meaning an accident with the potential to kill the whole industry or technology at stake) that experts had predicted for the industry, but it surely eroded the public confidence in the industry worldwide[5].
As noted by Ansell & Vogel (2006), the public controversy over GMOs has not been limited to the toxicity issue. It rapidly expanded and touched upon issues like the perceived dominant power of strong corporations over farmers, the consequences of trade liberalization, the globalization effects, the conservation of species and plants, and the free choice of consumers (Bray, 2003).
This highly political profile surely implies that the degree of monitoring and public oversight impacts greatly the very functioning and designs of the daily operations of such an industry. We could predict that if it were not the case at the moment, it will surely become a growing concern over the years for the management of this industry. As explained years ago by La Porte, the potentially highly publicized nature of any event or mishap is a burden, which in itself constitutes a risk (La Porte, 1996). Therefore, one can notice, that in such high profile industries tremendous efforts and substantial resources are targeted at either building or restoring public trust and confidence (La Porte & Metlay, 1996, La Porte, 2001). Some experts

[5] The yearly IRSN [Institut pour la Radioprotection et la Sûreté Nucléaire] barometer of the public opinion on risks and safety measures regularly such an erosion.

go as far as saying that the resources devoted to these activities are in fact counterproductive: they are diverting precious resources that could actually be more fruitful to the organization, including invested in safety devices. The efforts to appear transparent and open to criticism is seen as pumping a lot of energy, at the expense of vigilant but sober safety management[6]. From a different angle, Heimann is also bringing water to this mill. He suggests that the efforts that a company is putting to restore its safety after a big accident push to an almost "fatal" drift towards a risk of type II – a waste of resources – which will "naturally" lead to short cuts with safety in order to be able to produce in time what is expected. Heimann is describing this vicious circle as the biggest obstacle to sustained investments in safety (Heimann, 2005).

In many respects, the GMO industry is facing the same kind of challenge. Similar to the nuclear experience, there are parts of the world, where anti-GMO activists have destroyed GMO experimental fields (French activist José Bové attracted a worldwide fame for this action), whereas in other parts of the world the legitimacy of such crops is granted and established (Canada, USA). The "Nuclear-free zones" of the seventies mirror the "GMO-free zones" discussed in Europe and notably in Switzerland and in Russia, where areas like the Volgograd, Kostroma, Murmansk, Ryazan, Sverdlovsk or Ulyanovsk may possibly become "GM-free zones"[7]. As shown in the case of Brazil developed by Farias & Allain in chapter (X) of this volume, the GMO issue can even evolved over a 10 years period from a highly controversial issue to the suppression, at least officially, of the prior fears, for the benefit of a growing industry, operating under the "fight against hunger" flag. Following the analysis of Farias and Allain, this rapid conversion should be explained in the larger context of the influence of globalization over developing countries.

1.2. Uncertainty of the hazards

It is probably not accurate to say, that like the nuclear industry or the chemical industry, the GMO industry has the potential to kill, crippled or disabled in an instant hundreds or thousands of people. Still the uncertainties[8] at this stage that surrounds the

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[6] See on this point the controversy between Wildavsky and Perrow, summarized by Perrow in the *Afterword* of the second edition of *Normal Accidents*, 1999, pp. 366-368, See also earlier arguments in Nichols & Wildavsky, 1987.

[7] Olga Sobolevskaya, Food for thought: Russia joins the battle over GM products, *Organisation of Asia-Pacific News Agency*, March 7, 2007.

[8] As a recall, 7 types of risk apply to GMOs, summarized by Pretty in 2001: «1) Horizontal gene flows ; 2)New forms of resistance and pest problems ; 3) recombination to produce new pathogens ; 4) Direct and indirect effects of novel toxins ; 5) Loss of biodiversity from changes to farm practices ; 6) Allergenic and immune system reactions ; 7)

toxicity issue, the dissemination issue, and the mutagenic potential are calling for close monitoring of any adverse effect — StarLink and ProdiGene are two emblematic examples of such unwanted events —[9].

The mutagenic potential that GMOs are posing to the human body and to the environment is similar to the potential of radioactive materials. These are hazards where the time line question is particularly complex to evaluate, as the long term effects might not be measurable, or visible for years. In the case of GMOs, it might even been trickier: the genetic mutation induced by radioactive exposure is much more documented than the potential genetic disorders induced by long term ingestion of GMOs, or dissemination and cross pollination of GMOs (creating Superbugs and Superplants).

In this respect, the GMO industry along with genetic engineering could be considered as a high-hazard industry, because it is bound to adopt very strict and tight regulation in order to prevent, or deal with any unwanted consequences that at the moment are not totally envisioned, nor proven[10]. In addition, a failure during operations is not yet well characterized. For the moment storage mingling between GMO and Non-GMO products seem to qualify for a failure, but such an event does not prompt the same worry as a chemical spillover for example. It might be different for the third generation of GMO, the plant made pharmaceuticals, where the dissemination issue should be dealt with extra care. For that reason, the "precautionary principle" (duty of care) has been deemed applicable to GMOs and is still guiding political decisions in this matter, at least in some European countries (Bourg, 2001).

Again, it calls for a parallel between this new industry and older ones, in particular with respect to the uncertainties they are still carrying: for instance the effects of low radiation near nuclear power plants is one of those issues, as well as the slow poisoning and health effects on human beings (especially on the fertility rate) due to the heavy use of pesticides over the long run. One needs to mention of course that in those two cases, experts disagree (which does not mean that they deny the problems, but that they do not agree on the magnitude of the consequences). As they disagree on the two main issues regarding GMOs: the dissemination issue and the toxicity issue (we will return to this point in the second section).

Moreover, as in more traditional high-risk industries, this suspicion is so high in parts of the world that as La Porte has coined years ago those industries will in fact be subject to a

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Antibiotic resistance marker genes », in Jules Pretty, The rapid emergence of genetic modification in world agriculture: contested risks and benefits, *Environmental Conservation*, 28, N°3, 248-262, 2001.

[9] Stéphane Foucart, Forts soupcons de toxicité sur un maïs OGM, in *Le Temps*, p. 43, March, 15, 2007

[10] See, the following recent study : A Meta-Analysis of Effects of Bt Cotton and Maize on Nontarget Invertebrates, by Michelle Marvier et al, *Science*, 316, 1475, 2007.

"never ending management". La Porte applied the term to the operations of nuclear waste facilities, where tons of toxic radioactive wastes have to be stored for ages, regardless of the authorities in place at the time. Society has to be robust enough to actually make sure that such products will always be monitored with respect to the earlier engagements that former generations took for the future ones. GMOs have undoubtedly the potential to require to be treated with the same institutional care (La Porte & Keller, 1995).

1.3. Complexity, tight coupling, and failure

If we take the "classic" definition given by Rochlin (1993) for a High Hazard and Complex system – "High potential consequences, tight functional coupling and potentially rapid evolution of untoward events" – it appears that the GMO industry fits by and large with this definition.

According to Perrow's theory (1984, 1999), the more complexity and tight coupling there is in a system, the more safety is in danger. In fact, it could be extremely interesting to benchmark GMOs against Perrow's classic distinction between loosely coupled system and tightly coupled systems. GMOs seem to qualify for a rather tightly coupled system in the causal sense of the phenomenon. For example, once the seeds are in the fields, there is no turning back, no exit route: burn the crops is always possible, but it requires that the eventual safety problem has been detected in due time, i.e before the harvest. But they are also loosely or semi coupled in the social sense of it. The process itself is quite loosely coupled. Farms are spread all over the world. Since few corporations are holding the market of these plants, one could argue that there is an element of centralization, which will lead us to prefer the term semi-coupled[11]. But it is probably accurate to predict that it is a long shot before any international regulation of quality and safety aspects will take place.

The classical item "Buffers and redundancies fortuitously available" defended by Perrow as a major requirement for a safer design is especially of interest for our discussion. In the case of GMOs, these buffers could probably never be fortuitous. We cannot think at the moment of a future where some plants will naturally grow to contain GMOs, becoming a sort of a natural adaptation and protection to genetically modified organisms. The whole question actually is how to put these buffers in place rigorously with respect to two strong requirements. The first one is an economic one – buffer zones between GM crops and non-GM crops have to be kept minimal, in order to maximize land use and minimize GM farmers sunk costs. In addition, since in Europe, GM farmers are responsible for applying and bearing the costs of co-

[11] I thank Todd R. La Porte, from the University of California, Berkeley, for his help in pointing to me this dual characterization.

existence measure like buffers, they should rather be not too large if GM farmers want to make money (See on this Klaus Menrad's chapter in the book). The second one deals with safety requirement and has to do with the prevention of any adventitious presence of GM seeds in conventional ones. It will certainly gain in importance when the plant made pharmaceuticals will reach their full deployment. In this case, buffer zones have to be large and the distance between crops as big as possible. These precautions might not be enough, and other strategies are under discussions (we will return to this point later). As we can see, such dilemma is at the core of any concrete discussion on GMOs future in Europe for example, where the co-existence requirement is applied.

Following further Perrow's framing of the complexity issue, it is certainly true that there are "hidden complex interactions" in growing GMOs, notably those posed by the environmental reception of such crops. Some of these interactions are not yet foreseeable, because the collection of data is too limited so far. Some scientists are discontent with the present collection of data at their disposal[12]. Decades will be necessary to properly compare data and draw conclusions on potential negative effects of GMOs on wildlife, or biodiversity.

Last, we would argue that the relative spreading of the stakeholders increases the risk that safety might not be dealt with the required stewardship. The GMO industry is displaying a rather complex network of stakeholders that have interest in its deployment. The biotech firms (Mosanto, Bayer, Syngenta…), the farmers – those who are growing GMOs and those who do not want it, and who expect to be prevented from any dissemination incident in their fields –, consumers – those who do not bother, and those who bother strongly –, anti-GMO activists, independent labs, scientific experts from different disciplines (biology, toxicology, environmental sciences, agricultural economics…[13]) – who are bringing different angles to the question of the safety of GMOs, regulators – at national, federal in the case of the US or supranational level in the case of the EU –, politicians, to name the most important ones.

[12] As marvier et al put it: « Public debate regarding risks and benefits of genetically modified crops continues unabated. One reason for the unrelenting controversy is that disagreement about new technologies often have little to do with scientific uncertainty but instead arise from differing personal values and differing levels of trust in public institutions. However, in the case of GM crops, scientific analyses have also been deficient. In particular, many experiments used to test the environmental safety of GM crops were poorly replicated, were of short duration, and/or assessed only a few of the possible response (Marvier et al, 2007).

[13] For a very detailed account on the combination of these scientific points of view on these plants, and for the French case, see Alexis Roy, *Les experts face au risque: Le cas des plantes transgéniques,* Paris, La découverte, 2002.

We believe that this stewardship would require a minimal institutional centralization. We will return to this point later when we will address what we see as a potential help and benefit that the GMO industry could gain from adopting existing safety managing devices. One of them could be the implementation of events reporting systems, from minor ones to serious ones.

2. Unfolding the GMO Safety Model

We will now turn to the unfolding of the GMO safety model as we can grasp it through the various contributions that the book presents. This exercise in itself carries notable difficulties. The safety issue is in fact split in two distinct problems:
The first one deals with a toxicity issue: Will eating GMO products affect our health, modifying the functioning of certain organs, now or in the future (toxicity measures and tests are provided to assess this issue)?
The second one deals with the dissemination issue: Will growing GMOs affect the environment so much as to provoke substantial ecological changes in living species, in other categories of plants (ecological assessment can be realized but will need more time to be able to draw conclusions). Furthermore, will it reduce the biodiversity?
Historically the first one has been dealt with from the beginning in the early 80’ and the latter at the very end of the pre-market tests in the middle of the 90’.

2.1. A product safety model rather than a process safety model

So far, it appears that the safety assessment that is being performed by the various bodies in charge of the Food Safety standards, when authorizing GMOs on the market, has mainly focused on the intrinsic qualities of the product. It is especially the case for the American philosophy towards GMOs and less so for the struggling E.U philosophy, embodied by the European Food Safety Authority. What do we mean by that?
It appears that there is much consideration for the qualities and performances of the product in itself and less so on its possible interactions in the field with other plants and species or deteriorations of the product itself at the farms sites. The safety is envisioned in two ways: First, there is an assessment of the novel GM trait. For example, the safety of a particular protein regarding toxicity is assesses using animal feeding tests. Second, there is an assessment of the unforeseen changes in plant metabolism as a result of gene transfer.
Currently, in the U.S there is no obligation to organize for the farmers and growers a post market environmental monitoring. There is limited attention paid for the exact conditions under which such plants are cultivated, stored, exported, taken care of. There has been from the beginning of their cultivation a deliberate choice to treat them as any other food products (See Baram’s

chapter in this book). In addition, the various incidents that have been reported, concerning dissemination, cross-pollination, or commingling errors between storages, have not been directly life threatening for human beings. For many experts, these events are not classified as "safety-related" problems. Nonetheless, these events received a lot of public attention and scrutiny, especially because they are suddenly exposing to the world the hidden face of the whole process: i.e. the daily operations at the production sites. Human and organizational factors are suddenly back in the loop, inviting themselves in the debate. As Armin Spök is warning us in his eye-awakening chapter, those human and organizational issues will not be ignored for long, as they constitute the challenges of the development of plant made pharmaceuticals. These crops should not be found by accident in the food and feed chain because unlike first generation GM crops, plant made pharmaceuticals are designed to have a biological effect on man or animals health and well being.

As we just mentioned above, it is less true for the E.U recommendations. As an illustration of our point, we are referring here to the "Opinion of the Scientific Panel on Genetically Modified Organisms on the Post Market Environmental Monitoring (PMEM), adopted on January, the 25th, 2006"[14]. Indeed, when we read it carefully, an ambiguity emerges. If the first sentence is quite clear "A plan for Post Market Environmental Monitoring (PMEM) of genetically modified (GM) plants is *mandatory*[15] in all applications for deliberate release submitted under EU directive 2001/18/EC and EU regulation 1829/2003", the further developments in the opinion weaken the point: "PMEM is composed of case-specific monitoring and general surveillance of GM plants. Case-specific monitoring is *not obligatory*[16]but may be required to verify the environmental risk assessment, whereas a general surveillance plan must be part of the application", continuing with "The GMO panel concludes that general surveillance can not be hypothesis driven, but *should when possible*[17], make use of existing monitoring systems in addition to more focused monitoring systems (e.g farm questionnaires)". The wording is in fact limiting the impact of the first sentence. We understand implicitly by reading those lines that the PMEM is not yet a standard practice among growers and farmers. The organization itself of the GMO production is not included in the framework of any safety assessment. Safety management has not (yet) reached the shores of the production at farm sites.

This remark is further supported by the type of safety assessment, the "substantial equivalence principle" that is currently accepted

[14] "Opinion of the Scientific Panel on Genetically Modified Organisms on the Post Market Environmental Monitoring (PMEM), adopted on January, the 25th, 2006", *The EFSA Journal*, N° 319, 1-27, 2006.

[15] Underlines are mine.

[16] Underlines are mine.

[17] Underlines are mine.

as state of the art for the market authorization of GMOs. This will constitute our next section.

2.2. *The implications of the substantial equivalence concept*

The "substantial equivalence concept" explained in the book by Marianne Shauzu (chapter X, this volume) is cardinal. Essentially, the demonstration that has to be made before the regulators in order to be granted market authorization revolves around a systematic comparison between the properties of the GMO derived food with existing, "natural" products used as food or food sources. As stated by Marianne Shauzu: "It is based on the idea that existing products used as foods or food sources can serve as a basis for comparison when assessing the safety and nutritional value of GMO derived food. It implies that if the modified food is found to be substantially equivalent to an existing food or food component with regard to phenotypic and agronomic characteristics and chemical composition, it can be treated in the same manner with respect to safety" (p. X).

Earlier in the history of GMOs, molecular biology has been paramount and almost the unique science that was able to scientifically evaluate and authorize experiments throughout Europe (for example) in the late 80's and early 90's. At the time, the argument made was that the safety of GMOs is essentially determined by the quality of the molecular construction. The better and duly described by firms seeking approval for tests, the safer the construction will be, according to the biologists. Moreover, the idea that the construction had to be as simple and elegant as possible to be deemed safe has also contributed heavily to build a type of safety assessment, based on the intrinsic qualities of the new plant itself (See for a description of the French Commission of Biomolecular Engineering, the "CGB", the book of Alexis Roy, 2001).

The second term of reference is then a "natural" product that does not need to be assessed because it has already been cultivated for decades (or centuries) and has no history of toxicity. For many experts, a GMO after all is just another plant. For most of them at the time, a GMO was structurally safer because a complete traceability of its construction could be detailed and provided. Explicitly the dominant philosophy is that GMOs are much more controlled than existing plants, enhanced by less rigorous techniques, hence, much safer (Kahn, 1998)[18].

One of the implications of such pragmatic vision of safety is that it focuses mainly on the plants' characteristics, and neglects the interaction of such plants with existing ecosystems, not to

[18] For a very convincing brief on this philosophy, by one of the world leading expert, see Axel Kahn « Génie génétique, agriculture et alimentation : entre peurs et savoirs », (57-70) in Marian Apfelbaum (ed.), *Risques et peurs alimentaires*, Paris, Editions Odile Jacob, 1998.

mention the employees responsible for growing them, or the organization designed to produce such crops.
This choice from the beginning had to be reevaluated when growing concerns emerge from experts who brought on the table the blind spot of this new technology: the integration of such plants, when sowed on large fields with their environment and the necessity to address current agricultural practices. So far the safety evaluation of GMOs had been conducted without consideration for farmers and growers. Industrials claimed that it was their responsibility to watch over this issue[19]. In the early 90' market authorizations seem far away for experts and their model of reference was still the lab, with its biological containment possibilities (pollen tunnel for example), and decisions to destroy small experimental crops in case of a problem. Studying pollen flows had not been at the time seen as a priority.
Suddenly, market authorization had to be granted and the bio-vigilance emerges as a new and inescapable pillar in the safety assessment.

2.3. *The dissemination issue, Crops co-existence, Cross contamination*

Finally, ten years ago the safety assessment of GMOs had to incorporate these hazards. In Europe, the controversy over such problems only emerged in the middle of 90's, when the Belgian firm, Plant Genetic System (GPS), seek authorization by the British authority for its colza in 1994. It is only then that Bio-vigilance appears as a major part of the safety assessment of GMOs[20]. This rather late emergence is rooted first as we explained above in the predominance of molecular biologists at the early stages of the evaluation and second in the type of experiments that had taken place so far. Biological containment, like "pollen proof" tunnels and limited interaction with other fields were the norm. Third, it appears that the consideration for exact agronomic practices were outside of the competency and mandate of the traditional bio-molecular experts.

— *Classical buffers*

The dissemination issue brings on the table a classic safety problem, revolving around the issue of putting in place buffers and system barriers. The truth is that providing for an efficient

[19] Interestingly enough similar claim has always been made by the nuclear industry when asked for example to precise the way it will screen and monitor the skills of their employees. Even in heavily regulated industries, some domains are beyond the reach of regulators.
[20] « Le traitement de la sécurité des plantes transgéniques ne relève ainsi plus exclusivement de la qualification du risque au niveau des structures moléculaires. Le risque est désormais pensé à travers l'utilisation de ces plantes dans des conditions agricoles » (A. Roy, op.cit, p. 198).

strategy against wind blows and bees is probably much more complex than containing the activities of a high-risk technology (Well, not quite of course!).
In other high-risk industry where the dissemination issue is critical, because it directly relates to radiological contamination, chemical spills, or toxic effluents, several notions are used. Along with the “safety zones” or “exclusion zones”, the notion of “defense in depth”, historically coming from the nuclear industry, combines several types of barriers[21]. At first, the “defense in depth” was almost exclusively seen as technological by nature. Now it is understood as a much more complex notion, mixing technology, procedures, organization, communication and individual behavior. The “modern” defense-in-depth concept has gained (at least) from two sources: a) The rich results of the human factors research on categories of errors and mishaps, which lead to more effective errors prevention and mitigation strategies (Reason, 1990; Amalberti, 1996); b) The observations and theorization of the High Reliability Organization project’s early work, which point towards aspects of organizational life, that are crucial to promote innovative risk mitigation strategies (La Porte & Consolini, 1993; Rochlin, 1998; Rochlin, La Porte & Roberts, 1987). Of course, such decisions to diversify the barriers have been heavily influenced by the findings that numerous accident investigation commissions brought to light: Big accidents were rarely triggered by a unique, isolated human error, as it was often pretended in the past. Nor was it only triggered by a faulty technology. On the contrary, organizational factors played a crucial role in the fatal development of catastrophes, such as Chernobyl, Bhopal, the two losses of the NASA shuttles (Challenger, 1986, Columbia, 2003, See Vaughan, 1996), or the contaminated blood affair in the 90’ (Setbon, 1993), to name only a few. For most safety experts, the organizational factors are the next frontier to be addressed if one wants to see continuing progress in safety in high-risk industries. These hard-to-achieve progresses will guaranty that their central role in the functioning of our societies, despite the risks involved, still found support.
Rapidly, the first barrier is constituted by the *physical or technological barriers*, essentially through the design of the technology itself[22], and also by the provision for massive concrete walls, explosion and fire proof structures, earthquake proof structures, or spills receptacles (containment); *Administrative*

[21] For an up-date of the notion, alas in French, see Jean-Louis Nicolet « la défense en profondeur ou comment limiter les dégâts », *Annales des Mines, Réalités Industrielles, N° spécial Sciences et Génie des activités à risques,* Mai, 40-44, 2003.
[22] In the case of nuclear power plants, as a first barrier the nuclear materials are encapsulated in zirconium metallic tubes, then the reactor has an inox envelop, and thirdly; massive concrete walls are protecting the whole mechanism. That arrangement makes for the historical “defense in depth” of the nuclear industry.

barriers constitute a second line of defense, carried through detailed procedures, that describe the exact functioning and limits of functioning of each safety organs; *Organizational barriers* are forming a third defense. They describe the exact responsibilities of each category of employees and provide for a description of key processes along with the division of labor in various situations, from the routine production mode up to the accidental one and through the degraded mode that goes along with these processes. Formal communication flows and standardized language engagements are also addressed, as well as the need to encourage formal and informal debriefing and conditions to exchange freely on surprises. Finally*, individual barriers* provide for adequate training, personnel selection and specific licensing. Those industries have put in place access limitations and diverse devices (alarms, warning devices…) if and when there is a breach of one of the defenses. The key point is to provide the first-line actors with an up-dated picture of the state of the system at all times.
It is of interest to note in passing that the medical field is also interested by this line of thinking and struggle to put in place system barriers, capable of reducing successfully preventable errors (Amalberti *et al*, 2005; Carroll & Rudolph, 2006).
This description is not aimed at pretending that those barriers are sufficient to guaranty operational safety. Of course they are not. The whole debate after Chernobyl led to the recognition that much more was needed to actually operate such complex systems and ensure reliability and safety (La Porte & Consolini, 1991; Schulman, 1993; Bourrier, 1999; Bourrier, 2001, Weick, 1987; Weick & Sutcliffe, 2001). The idea here is to envision what could represent parallel efforts to tackle the dissemination issue for GMOs farmers. What could be a defense in depth for GMO production? Where are the barriers?

— *Defense in depth for GMOs?*

The reality of such a “defense in depth” for this kind of productions should certainly not be envisioned in the same way as the more traditional “defense in depth” in place in high-risk Industries. Building fences against gene flows and winds remains a challenge. But the difficulty should not prevent the various actors to go forward finding acceptable precautions, which could contribute to build a modern hazard mitigation strategy.
Several ideas have been brought in[23]. They could be interpreted as an embryonic defense in depth. They have essentially been evoked in the context of plant made pharmaceuticals.

♣ The first technological and physical barrier

[23] I thank my colleague Claudine Burton-Jeangros from the University of Geneva, for pushing me to clarify this section.

As an example of a first barrier, functioning like a “natural” containment, the provision that plant made pharmaceuticals will only be hosted by non-food/non-feed crops (like tobacco), hence reducing the risk of contaminating the food/feed chain, has been discussed. Another barrier, technological by nature, is the provision to only design and manufacture plants that do not reproduce through pollination. These two provisions relate to “safety by design” strategies.
In addition, the set-up of a closed system for the production (contained conditions and no chance of open pollination) using hermetic greenhouses qualifies for a physical barrier. The destruction of the crop after the extraction of the protein constitutes also a physical barrier to prevent any unwanted mutation.
A forth element, included in the first barrier type, uses agronomic techniques: Co-existence measures like crops rotation, cultivation in remote areas, buffers zones between GMO fields and non GMO fields exist already and could serve as an interesting addition to a more complete arsenal.

♦ The second organizational barrier

The organizational barrier that exists in traditional high-risk industries has not yet been fully laid out in the context of GMO production. We have no information on the way operations are organized at farm sites. Who are the “first-line operators”, how are they organizing themselves? Who’s in charge of attending to surprises, dissemination issues, commingling, errors of storage, safe disposal or destruction, recycling of biomass, surveillance of the interactions with the environment? How the division of labor is done and what is the implication for the successful production and delivery of the products in the end?
There is no doubt that these organizational factors will come under scrutiny in the case of a severe contamination incident, with potentially negative health effects. But so far, as in early periods of “classical” high-risk industries development, emphasis on these issues has not been seen as a priority. There is no organizational thinking so far as GMO production is concerned.

♠ Third barrier: written procedures

Armin Spök, in his chapter, is giving us examples of several Standard Operating Procedures that are currently discussed or proposed by the US Department of Agriculture. They are only proposed in the case of plant made pharmaceuticals, but could well give ideas for first generation GMOs.
According to his information, Standard Operating Procedures will be developed for seeding, transplanting, harvesting, cleaning, storing, dying, processing of biomass…They will also regulate the use of the machinery, and promote dedicated use of machinery. This

sole list convinces us of the various activities conducted at farm sites, and their importance in a safety perspective.

♥ Human barrier

In line with our comment on organizational factors, there is no information on the characteristics of the farmers, attending to the GMO production. No information on the requirements that corporations or agricultural firms have put in place for the recruitment and the specific safety and quality training provided to their employees. No doubt that such issues could potentially become important in the case of unwanted errors and mishaps.

☮ Conclusion

Despite some elements that are already discussed, there is not yet any systematic hazards mitigation response, combining technological, physical, organizational and individual barriers that could match what exists in other high-risks Industries.
To understand this state of mind, one would recall that the dissemination issue is not seen in terms of safety by some of the experts. Which might explain why a coherent response has not yet emerged. The dissemination problem is rather presented as a consequence of a consumer requirement – European essentially – the free choice. Therefore buffers or rotation zones are not envisioned as a measure of risk mitigation to contain/prevent/reduce the possible adverse effects of products, whose interactions with the rest of the environment are yet to be understood. They are only tolerated and promoted as a market requirement. However, one can notice that this is currently changing in the context of the plant pharmaceutical development.

Conclusions: Propositions

Bringing the people back in

The Standard Operations Procedures (SOPs) that seem to emerge in the context of Pharming could be also applicable to more traditional GMO cultivation. It could constitute a first response to the growing demands over a more systematic traceability and…safety. This effort could bring back in the loop, a keen interest on agricultural practices and a necessary consideration for organizational and human factors that have been so far neglected throughout the process.
However, the march towards SOPs should not become an alibi and be the unique response to a broader perspective on human and organizational factors. As the examples of other industries have taught to a vast community of experts: one can only achieve part of the goals by designing procedures. There should also be a consideration for the various factors that play a role in fostering safety culture at the farms' sites and along the

commercialization process. Attention given to organizational issues at farm sites and a better understanding of the sociology of GMO farmers and their institutional environment are two key aspects of a possible step towards this goal. It is also the only practical way to prepare for a response in case of a damaging event. So far, the public has no knowledge on the organizational and institutional conditions for this industry to recover promptly from a problematic event. “Bringing the people back in” and develop interesting studies on the day-to-day operations at farm sites will also contribute to adopt a new perspective on this technology too often only considered through the lenses of laboratories wonder, when not seen as a potentially harmful technology.

Collecting unwanted events and sharing them?

The other tool that could be put in place addresses the question of developing a systematic reporting of unwanted and adverse events (such as contamination of non GMO crops; Commingling at storage sites; Gene flows…). It appears clearly that this kind of effort would require assuming for the industry and the regulators a stewardship role that seems lacking at the moment.

The nuclear industry as well as the civil aviation has now developed institutional links across countries and companies (even imperfectly) that assume this stewardship role[24]. The chemical industry is struggling to put in place such a formal exchange of information, as truthful as possible. Industry patents and trade secrets are strong obstacles to such initiative. The same kind of obstacles is certainly at the core of the wariness one can perceive in the genetic engineering case.

However, such efforts have gradually been considered as mandatory after severe accidents have shaken not only the very company, which operated the responsible site or plant, but the whole industry. As if the perspective of having to suffer from bad operators prompted each of these High risks industries to organize its own vigilance (Rees, 1994). After the AZF devastation in Toulouse (France), in September 2001, similar observations had been made, regarding the absolute necessity to organize a much more powerful errors and events reporting system, shared among the main industry players.

The fact that NGO’s, and anti-GMOs activists are putting in place websites collecting data on various incidents regarding the GMOs could also be a strong motivation for the industry to organize

[24] For the Nuclear industry, several institutions are assuming this stewardship role: IAEA, the International Atomic Energy Agency, a United Nations Agency based in Vienna, INPO, the Institute of Nuclear Power Operators in the US, WANO, the World Association of Nuclear Operators, WENRA, the World Association of Nuclear Regulators. In the case of the civil aviation, the International Civil Aviation Organization is a strong equivalent.

itself at a more generic level in order to provide its own forum of exchange and data collection, notably on unwanted and adverse events.

Where lies the GMO production safety model?

To answer this final question, we have been comparing this technology, with what we call “classical” high-risk industries on one hand (Nuclear power plant, Chemical plants, civil aviation…), and the Medical Field (hospitals…) on the other hand. Collecting the various dimensions introduced in the chapter, we have summarized the results in the table below. It appears clearly that the degree of maturity regarding the human and organizational factors issues in the safe and reliable development of the GMO technology is low compared to the other two cases. Interestingly, the medical field, where failure is accepted (less and less so) and death always possible, as opposed to the GMO industry, where failure would not be tolerated, is far more advanced in the recognition of the crucial contribution of team work, communication, and organizational dimensions in the “production” of a safe care, than the GMO industry. As the table shows, the progress margins are important for the GMO industry. It could certainly benefit from programs developed for other high hazards industries. For one thing, the political pressure and the public scrutiny will probably force the biotech corporations to initiate some actions in this direction. But, more importantly, we believe that the requirements in term of quality and safety of the end-products (GM, as well as Non GM), and those of the plant made pharmaceuticals will probably oblige the companies to attend to the “soft” issues and skills, because they are at the core of any safe production. Even more significant than the biological characteristics of a particular GMO are the conditions of its production.

Table 1
Properties Accross Industries

“Classical” High Risk Industries ✈	Medical field ✂	GMO production ✿
Contested Technology	Consensual	Contested technology

Some risks are wel documented and known Some uncertainty	Uncertainly of the cou of action	Uncertainty of the hazards
Operational errors can be characterized	Operational errors are sometimes difficult to characterized	What is an operation error?
Failure unacceptable	Failure acceptable	Failure unacceptable
Death is not expected	Death is possible	eath is not expected
Rather centralized	Rather decentralized	Rather decentralized
Highly regulated (Process regulated	Mildly regulated	Mildly regulated (Product Or Process regulated)
Safety in design	Some safety in design	Some safety in plant design
Systematic defense in depth	No defense in depth	No systematic defense in depth
Physical Containment	No Containment	"Natural" containment a) Pharmaceuticals in tobacco cycles and rotation Physical Containment : Greenhouses… to virtually none
No fortuitous buffers	Informal recovery	o fortuitous buffers
Presence of Incident Reporting Systems (IRS)	Some efforts towards he instauration of IRS	Absence of Incident Reporting Systems
Numerous SOPs (Too many?)	Some SOPs (Too few?)	No SOPS (Some under discussion)
Organization Seen (now) as an essential contribution to saf	ganization: still seen a a burden	What organization?
Operators center	Patient Centered at best	Operators absent
ganizational culture Seen as a key Safety element	Organizational culture More and more seen As a key safety element	What organizational culture?

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