# Chapter 6

## Understanding the uncertainties arising from technological interventions in complex biological systems: The case of GMOs

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Technological control of and intervention in complex biological systems inevitably create risks and concerns about unexpected or unidentified outcomes. The lack of empirical data (evidence) and scientific consensus, as well as the various types of uncertainty embedded in dynamic biological processes limit the knowledge sources regulatory agencies can draw on to effectively assess the health and environmental impacts of novel technologies. Thus, contested scientific knowledge, and intrinsic uncertainty surrounding biological processes create an arena where the lack of conclusive evidence can serve differing interests. For instance, industry can advocate the beneficial impacts of their novel products whereas other interest groups, claim that application of the same products involves unacceptable risk to health or the environment. The divergent groups may all present rational agendas given their contrasting risk-benefit perspectives, objectives and values within the dynamic discourse of knowledge formation. The commercial introduction of genetically modified organisms (GMOs) has revealed a broad range of views among scientists and stakeholders on risk perspectives and if and how GMOs should be regulated. The 'science-based' risk assessment of GMOs has resulted in different policy outcomes dependent on how the regulatory agencies involved have assessed various types of, or lack of, data to reach conclusions in the face of uncertainty. In this chapter we describe and contextualize the broader scientific uncertainties present in the process of risk assessment of GE and GMOs. The discussion is structured as follows:



### *1. Lack of scientific understanding of the biological processes involved and affected*

Uncertainty is the driving force of science and hence there will always be tension and a time-lag between the science-based regulatory agencies' immediate need for robust knowledge and the relative, iterative process of knowledge production itself. In many cases, especially with new technology, the regulatory decision making is done in the absence of 'certainty', and hence it is vulnerable to various types of subjective assumptions about the risks and benefits involved. The types of uncertainties surrounding GE and GMOs can be divided into three broad classes:

(i) Reducible uncertainty, due to lack of knowledge and the novelty of the activity, which can be addressed with more research and focused collection of empirical data.
(ii) Irreducible uncertainty due to inherent randomness, variability and complexity in the biological system under consideration.
(iii) Uncertainty arising from ignorance given that the prevailing operating paradigms and models do not adequately represent the biological system evaluated.

A holistic approach to the potential risk issues of GE and GMOs involves appreciation of these various types of uncertainty and encourages its explicit consideration and communication. This can be challenging and controversial because a holistic approach often questions the basic assumptions behind the science, i.e. problem framing, hypothesis formulation, model choice, and the use of and reliance on specific methods and assumptions for data production and interpretation (Section 1.1), the extent to which reliable, reproducible data can be obtained at all (Section 1.2), and whether the prevailing paradigms in which data are produced are sufficiently representing the system investigated so that no unforeseen effects will materialize (Section 1.3).

### *1.1 Uncertainty in data quality and production*

***Data quality.*** Access to peer-reviewed quality data is essential for a 'science-based' risk assessment. In order to gain regulatory approval, commercial developers of GMOs often submit their own test results to document the expected behaviour of the GMO and its products in the exposed system, and hence, its safety. Some experimental data on the safety of GMOs are also available in the peer-reviewed literature (Vain, 2007). Yet, knowledge gaps are routinely identified during regulatory risk assessment of GMOs. These gaps are often due to missing data (lack of relevant studies) or because the previously published studies have too narrow a scope or have focused on aspects of the biological system with only limited relevance to the biosafety of the GMO itself. To address the lack of direct empirical data and studies, a number of substitute approaches and assumption-based reasoning are routinely included in regulatory risk assessment. Often, the concepts of *familiarity* (with the unmodified parent organism) and *substantial equivalence* (to the unmodified parent organism) are used to frame the safety investigations of the GMOs in the context of previous experience and current analytical methods (König et al., 2004). These concepts are developed and maintained within expert cultures and evaluations of the GMOs. Thus, inference, drawing from organismal history and comparative experiences and observations of the parent organism (of both the GMO and the GMO trait itself), form the starting point of all current risk assessments of GMOs.

Regulatory risk assessment is based on literature reports of evidence (data) and not on data produced independently by the regulatory agency itself. The data received by the regulatory agency is thus produced and contextualized within the objectives that initiated the study (e.g. to support the safe commercialization of the GMO). Due to the many potential sources of motivational bias in directly submitted (often with confidentiality claims) and peer-reviewed data, it is essential that the multitude of data sources used, and the inferences and assumptions made in the risk analysis are openly evaluated and clearly communicated (Marvier, 2002; Lövei & Arpaia, 2005; Meyer et al., 2005). Accordingly, the outcome of any risk assessment can be no more conclusive than the quality of the underlying data. This reliance on data quality and external providers of data seems often to be forgotten in the scientific debate on risk issues of GMOs; providing the ground for subjective expert opinions and value-influenced interpretations to provide the main 'data' basis for the arguments forwarded.

***Data production: hypothesis formulation.*** Hypotheses define the problem framing that underlies all peer-reviewed research that in turn yields the data subsequently supporting the biosafety assessment of GMOs (Jewett, 2005). Understanding the processes behind hypothesis formulation

is thus critical for conceiving how scientific data are produced and peer reviewed. The subsequent downstream choice of models and methods used for testing the hypothesis also depends on the hypothesis itself. Because an unlimited number of hypotheses can be constructed for any given problem, an equally unlimited number of model and method choices are at hand. This is clearly the Achilles heel of science, as hypothesis development is limited to the researcher's preconceived ideas of the system and the paradigms within which the biological system are understood (Strohman, 1997). Moreover, the researcher's ethical values, research environment, funding sources, employment status and financial prospects, time constraints, and material/resource accessibility will influence if not determine the biosafety-relevant hypothesis generated (Lewontin, 1991). Thus, subjective choices and motivational bias in conceptualization of the hypothesis behind the research question (risk identification) may far exceed the uncertainties in the specific experimental design and data collection itself.[1] There are no internationally agreed upon detailed standards for the methods used for biosafety-relevant data collection[2]; partly due to the case-by-case nature of risk assessments and the large geographical differences in ecosystems. Thus, the quality of biosafety data must be understood and interpreted in the research and motivational context within which they are produced. Likewise, the absence of biosafety data may indicate ignorance, or a lack of or bias with respect to research focus, motivation, capacity, time, or financial or political research support.

***Data production: choice and limitations of models.*** In most scientific studies, models of a biological system are designed to test hypotheses about a phenomenon, or a specific cause-effect relationship (e.g. an intended or unintended effect of a GMO). The assumption is that the model represents the natural system with respect to the relevant parameters measured. By definition, a model does not claim to represent the 'truth' and therefore cannot be argued to be false. In contrast, hypotheses are directly linked to the natural system and are falsifiable. There is at present little scientific consensus on the choices of models and methods to investigate the effects of GE and GMOs; this concerns both the proposed benefits and the undesired effects. This scientific uncertainty arises from incomplete understanding of the interactions among natural variables and the limitations inherent in simplified models in predicting the behaviour of multivariable natural systems. For instance, the potential for pollen flow from genetically modified (GM) crops to other crops, weeds and wild relatives is a biosafety-relevant question for regulators and scientists that can be addressed by a range of hypotheses and model choices of a highly complex natural system. Pollen flow raises issues such as:

- Economic and legal concerns with regard to how GM crops can be cultivated in co-existence with conventional and organic farming, including issues related to labelling, liability, and socio-economic aspects such as effects on traditional farming practices, product identity, seed quality control, and changes in farming infrastructure.

- Environmental concerns with regard to potential adverse effects from flow of transgenes (introgression) into cultivated species, weeds and wild species.

[1]For example, a company researcher holding a utilitarian view that GMOs are a simple extension of traditional breeding efforts would develop biosafety-relevant hypotheses that are likely to be quite different from a researcher with a previous background as an environmentalist viewing GMOs as novel entities with little in common with traditional breeding. Both researchers will develop biosafety-relevant hypotheses, but it is clear that these would differ substantially in the problem framing, resource requirements, models and methodologies, data interpretation and contextualisation, and hence, possibly in the outcomes.

[2]The Codex Alimentarius (2003) represents a collection of internationally adopted food standards, including principles for risk analysis and guidelines for safety assessment of foods derived from modern biotechnology. Environmental, ethical, moral and socio-economic aspects are not addressed in the Codex standards.

- Health concerns with regard to the potentially changed allergenic properties of pollen caused by the genetic modification, or health impacts caused by pollen flow from GM plants producing pharmaceutically-active compounds into crop plants entering the food chain.

These concerns can be seen through risk windows of many sizes, addressed by a number of hypotheses on the effect (or lack thereof) of GMOs on agriculture, and investigated with a broad range of methods and scales. Recently, farm-scale field trials on the biological effects of GM plants (compared to non-GM varieties) have been performed (Squire et al., 2003); an approach that certainly broadens the scope, system reliability and robustness of the data produced.

***Data production: choice and limitations of methods.*** In the conducting of research, scientists make assumptions and inferences based on the paradigms within which they are trained and the research environment they are socialized into (Kuhn, 1962). The choice of models and methods to test a specific hypothesis is a variable of the research environment, resources, the competencies and instruments at hand, and most importantly, time constraints. Thus, researchers operating in different research environments will invariably choose different models and methods to address the same risk-relevant question. An example is the issue of addressing potential allergenicity of GMO products. This issue is exceedingly complex, and the mechanistic aspects of allergy development are not fully understood, even within the basic medical sciences. Thus, there is no single biological model or experimental standard available to evaluate the potential allergenicity of new products from GMOs.

Scientists have thus been drawing on the familiarity of the unmodified host organism(s) and have constructed a number of models, assumptions and comparative approaches to justify the claim of absence of allergenicity in GM products.[3] Not surprisingly, the assumptions behind selecting the most appropriate model and method choices have been questioned (Spök et al., 2005). There are few alternatives to testing in live organisms. Yet, selecting live test organisms, other than humans, inevitably raises questions about the relevance of the animal model chosen because there is no single animal model that can reliably solve allergenicity questions in humans. The choice of model system and methodological approaches will likely remain a contentious issue in the pre-marketing investigations of the safety of GE and GMOs.

It is important to be fully aware of the limitations of the methods and models used when considering and concluding from the outcome of biosafety-relevant studies (Andow, 2003). Often, various interest groups (sometimes also the 'objective' scientists behind the study itself) are eager to conclude more broadly from the studies than what the applied methods, models and produced data allow. The assumptions underlying the study, the choice of hypotheses, the interpretation of published data, as well as the significance of the absence of data, can lead to unsupported claims about the intended or unintended effects of GMOs. For instance, one frequently hears that 'there is no data to suggest that unintentional effects occur'. Such an argument raises two questions:

1. Have relevant studies been done *at all* to produce data that address the question?

[3]These include (i) computer-assisted bioinformatics-based comparisons of the new proteins (produced by the GMO) to known protein allergens, (ii) examinations of the stability of the protein in experimentally simulated gastrointestinal tract systems, and (iii) experimental and theoretical consideration of the overall concentration, composition and stability of the protein (e.g. heat stability). It is clear that these methodologies require numerous subjective decisions regarding the exact experimental conditions applied. Some examples of assumptions that depend on the model choices include assumptions that the allergenic site can be identified in proteins based on 2-D amino acid composition and not 3-D structure, and that the protein digestive capacity of the gastrointestinal tract of humans can be adequately constructed by mixing specific concentrations of enzymes and chemicals in test tubes.

2. If studies are available, what were the motivations, objectives and hypotheses behind the production of the data, and are the tested hypotheses, models and methods sufficiently robust to support such a statement?

An example of this type of argument, not infrequently also found written in biosafety risk assessment documents, is 'there is no data to suggest that plant transgenes have transferred horizontally into bacteria'. It is often unclear if such an argument is made because the authors have examined the range of peer-reviewed studies that have used suitable methods to produce risk-relevant data, or simply that no relevant studies have been done and considered in the assessment.[4]

In conclusion, beyond the explicit awareness and communication of the rationale behind the risk conceptualization, hypothesis formation and choice of models and methods, scientists must clearly communicate the limitations of their methods and experimental approaches. Likewise, regulators must explicitly consider the problem framing behind the hypothesis construction, the context behind the model choices, and the methodological limitations embedded in the data when drawing on experimental studies in risk assessments.

### *1.2 Indeterminacy due to inherent randomness in biological systems*

Biological systems are highly complex and may not be easily quantified or explained by quantitative methods. Random variation in baseline data in conjunction with complex, multi-scale network interactions between molecules, cells, organisms, physical environments, and environmental variables (temperature, season, geography, etc.) can lead to meaningless quantification efforts; and hence indeterminacy (Funtowicz & Ravetz, 1990; Wynne, 1992). Whereas precise numbers (such as the rate of gene flow, or degradation kinetics of a protein) can be obtained within various experimental model systems, their quantitative mean and range as a variable in changing geographical and environmental contexts rarely have the same level of precision.

Regulatory decision makers often face exact numbers presented in experimental data, but in reality, robust range estimates are unachievable.[5] The regulators or scientific advisory board must therefore make judgments as to whether to base the assessment on the empirically-determined numbers at hand (given the limitations of the models and methods by which they were obtained), or make their own subjective predictions of the number ranges in real life.

[4]Re-examining the available literature on monitoring gene transfer from plants to bacteria, two groups of scientists independently concluded that previous studies that have examined this risk scenario have used methods that are unable to resolve the issue (Heinemann & Traavik, 2004; Nielsen & Townsend, 2004). It was found that the currently applied sampling methods for monitoring of gene transfer from GM plants to soil or human intestinal gut microorganisms are too insensitive and effectively have only examined a few grams of sample material from the gut or soil. These severe limitations in the data were not previously exposed in regulatory risk assessment documents.

[5]Consider, for instance, the example of gene flow from GM bacteria to wild-type bacteria. Laboratory models readily provide the opportunity to quantify gene transfer frequencies between defined bacterial populations grown under simplified laboratory conditions. However, are these numbers (or even the absence of detectable transfer) relevant to the broad range of natural conditions or bacterial species these GM bacteria encounter? We argue, not at all. For example, published studies suggest gene transfer processes occurring in complex environments such as soil can vary more than a billion-fold, even within a gram of soil (Nielsen et al., 1997). This is due to the locally highly variable microhabitat that soil represents (soil types, plant roots, rock surfaces, animal manure, water logging, etc. (Nannipieri & Smalla, 2006)). Thus, laboratory-obtained numbers are most often irrelevant, and neither encompass the high spatial-temporal variation in gene transfer rates in nature, nor incorporate the effects of selection or genetic drift with equally constrained quantitative approaches (McHughen, 2006). Thus, most vertical and horizontal gene transfer frequencies remain practically indeterminable in all complex environments since the full set of environmental conditions cannot be fully conceived or examined.

A closer look at the quantitative aspects of biosafety-relevant studies reveals that indeterminacy is an intrinsic component in many, if not most, of these and hence they are of little direct quantitative value. Subjective assessments and supportive claims must therefore be constructed to support their informative value in risk assessments. For instance, given that pollen flow is shown to occur between GM and non-GM plants, frequency estimates of this process are only relevant to risk assessment if they are robust to variations in environments and conditions such that the process can be reliably quantified (McHughen, 2006). In most cases, this will not be the case as the measured frequencies represent a snapshot taken in a given farm-field context.

While we appreciate the value of numbers, they may be more useful to identify relevant processes for subjective assessment within a qualitative risk perspective. Nevertheless, risk assessment documents frequently make use of specific numbers drawn from empirical studies. Perhaps this is done unconsciously for the purpose of constructing an argument (providing exact numbers that erroneously give the impression of high accuracy) to support their final risk conclusions rather than cautiously communicating the context (and the associated uncertainty) in which they where produced.

In conclusion, complex natural systems have cause and effect relationships in multiple dimensions, therefore often making them untenable to current experimental methodologies that seek to produce exact numbers that can support quantitatively oriented risk assessments. Nonetheless, precise numbers quantifying risk-relevant scenarios remain the preferred support and basis for regulatory decision making, perhaps since this conveys an impression of numerical certainty in the assessment (Meyer et al., 2005).

### *1.3 Ignorance arising from conceptual limitations in the operating paradigms of the biological system*

Risk from GE and GMOs arises because there is uncertainty about casual chains in the intervened complex biological system. Yet, on the surface, successful applications of GM techniques appear to demonstrate an increased knowledge of the biological systems that have been genetically modified. However, intervening at more powerful levels does not imply that the intervention is more controlled. In fact, the intervention may increase the level of ignorance by widening the gap between the levels where human intervention is possible and the levels where accumulated knowledge, experience and consensus confer predictability on the processes involved and affected. For example, whereas the random introduction of novel DNA fragments into the genome of most organisms is now a routine technique in molecular biology laboratories, the corresponding knowledge and predictive power of the unintended cellular, organismal and environmental effects are only partially understood. Due to the lack of a coherent understanding of how genomes function, it is today impossible to predict precisely how the introduced genes will function in the new host organism and how the modification will affect the organisms' own gene functions and regulations (see Chapters 3 and 8). It is, with little scientific support, often assumed by GMO developers that the new transgene-encoded product will act independently of the many thousand proteins and metabolites active in the same cellular environment.[6]

[6]Yet, there are many examples of ignorance of unintended effects of transgene insertions (Cellini et al., 2004; Prescott et al., 2005; Filipecki & Malepszy, 2006), and without doubt most of those observed have never reached the peer-reviewed literature. This is because the reports on unintended negative effects (ignorance) available in the peer-reviewed literature represent only those experimental studies for which the authors (including the journal editor) have had a motivation to publish. Since most developers of GMOs are companies with no incentives or duties to publish negative research findings (i.e. that would create investor uncertainty on the safety and predictability of the core technology), it is clear that the published studies represent only a minor fraction of the observed unintended effects to date. Moreover, in GE-based plant breeding most undesired events are excluded from further breeding seasons (similar to traditional plant breeding programmes), resulting in exclusion of most events with undesired or unintended

An overriding philosophical concern with the scientific approaches applied to the reduction of ignorance in GE and GMOs is that current methodology directs and shapes the research questions raised in regard to details within the system itself (reductionism), often producing little coherent understanding of the larger system (holism).[7] The absence of a holistic research focus can be explained by relative lack of comparatively precise methods and inability to test a defined, detailed and single cause-effect based hypothesis. Moreover, the results produced from more holistically oriented approaches are necessarily with lower mechanistically based explanatory power, often less reproducible and not patentable due to inherent variation in the processes within and between organisms. Thus, due to a lowered immediate commercial potential they become less valued and attractive to pursue within the current single hypothesis- and patent-driven scientific approaches. In science philosopher Thomas Kuhn's view (1962), scientists work well within defined paradigms focusing on specific mechanistic (and therefore patentable) aspects of the system. Thus, it can be questioned to what extent discipline-oriented researchers and research institutions are effectively trained, organized and motivated to take on broad cross- and multi-disciplinary approaches that may be required to advance the broader understanding of the implications of technological interventions.

The ecotoxicological risk perspective (paradigm) has been influential in shaping risk concepts in biosafety. This unwittingly contributes to further ignorance since chemicals follow a different environmental route and degradation pathway than transgenes (Karlsson, 2006). Chemicals have a release-dependent concentration decline with a given breakdown time in the environment. In contrast, (trans)genes follow the path of the host genome, possibly eventually also the path of sexually compatible and some incompatible species (through vertical and horizontal gene transfer). Hence, the initial release concentration of the (trans)gene may have little predictive power of the persistence time, degradation routes, or amplification and spread of the transgene in the environment over time. Thus, ecotoxicological risk models (based on the premise that exposure dose predicts response) have no or little utility in predicting the environmental behaviour of released transgenes, where exposure dose does not predict response. This is explained by the conceptually different contexts and behaviour of the evaluated entities, i.e. non-replicating chemicals versus replicating genes and organisms.

*2. Lack of scientific consensus on the effects caused and observed*

There are divergent opinions among scientists about the occurrence and relevance of potential adverse effects arising from GE and GMOs, the definition of potential 'adverse effects', and what action to take (if required at all) to prevent potential harm (Myhr & Traavik, 1999; 2003). Various scientific experts draw or make inferences from their specific scientific disciplines to support their views and framing of the risk issues debated.[8] Because experiences and traditions, paradigms, problem framing, models, and methodologies differ sharply among scientific disciplines, there may be little common ground for single scientific disciplines to independently

characteristics. Several years of subsequent selection-based breeding of the novel GM plant events lead to an increase in familiarity with the event (plant cultivar) and hence, to a reduction in the level of overall ignorance.

[7]For example, there are massive efforts to elucidate and engineer single metabolic and signal transduction pathways within cells, but the corresponding wider perspective on how these pathways act in concert, within organisms, and respond to variations in the organism's environment, is less understood.

[8]For instance, agricultural biotechnologists often make inferences about the safety of GM plants based on the long tradition of safe use and predicted behaviour of and familiarity with conventional crop plants. Implicit in this is the assumption that the insertion of species-foreign genes does not substantially alter the genetics and physiology of the modified plants beyond the inserted trait. Some ecologists, on the other hand, refer to experiences catalogued from the introduction of exotic species to make inferences on the anticipated knowledge gaps about the novel GM plants that may only materialize as a negative effect after years of cultivation and widespread distribution. Implicit in this is the assumption that GM plants may have substantially different genetics that can produce unpredictable properties.

solve broadly framed biosafety concerns. Thus, while acknowledging the variation in the different disciplines' problem framing and risk conceptualization, the broad demand for 'more research' on biosafety issues is not necessarily sufficient to build consensus among scientists and stakeholders on risk issues and to reduce uncertainty.

In fact, more research may lead to increased uncertainty due to the discovery and exposure of novel processes and factors not previously considered that might also cast doubt on the adequacy of the scientific methods used in previous studies (Sarewitz, 2004). Yet, keeping in mind the subjective context of scientific practice and data production, few would disagree that continued research on biosafety issues would contribute to improve the safe use of GMOs. The lack of scientific consensus is a normal and often *the* driving part of science, and is not a particular risk feature of GE and GMOs. Sarewitz (2004) denotes this observation as an 'excess of objectivity', referring to the observation that available scientific knowledge can legitimately be interpreted in different ways to yield competing views of the problem and therefore differences in society's response. Meyer et al. (2005) argue that the current lack of data and the subjective constituents, particularly integral values, within data production in biosafety hinder scientific consensus building on the effects caused and observed. Moreover, a non-uniform response is seen among experts to new studies reporting deviations from safety assumptions further exemplifying the values, stakes and subjective interpretations underlying the discourse on the safety of GE and GMOs.

A main challenge in regulatory risk assessment is how to interpret and weigh conflicting studies of which some may indicate an undesired effect arising from the activity, whereas others, perhaps the majority, indicate no observable negative effects. Thus, in other words, should biosafety assessment be exclusively based on mainstream science and the leading scientists' views on what type of studies to pursue and their interpretation of data? Further, how should contrasting data and minority views be communicated in the conclusions of a risk assessment?[9] There is no clear policy on how to deal with contrasting studies during regulatory risk assessment, leaving their inclusion or exclusion, and interpretation open to subjective assessments made by the members of the regulatory body. Often, the presence of conflicting safety studies in the regulatory risk assessment phase may never reach the risk communication phase, due to the perceived need of providing the public with an unambiguous risk conclusion that is not intended to communicate that there is uncertainty.

### *2.1 Disagreements between experts on data interpretation and 'sound science'*

How can experts disagree on study design and the interpretation of data if knowledge production itself is the outcome of unbiased rational thought and approaches? Postmodernist philosophers question whether scientists can ever be neutral and objective. The subjective components of science in hypothesis construction, experimental design, data interpretation, contextualization, and communication are rarely as heavily exposed as in the discourse on the biosafety of GMOs. The idealized view of an objective approach in science has long been dismissed by the philosophers of science and by those scientists taking a broader interest in their own field of research. For instance, more scientific journals now have a strict policy requiring scientists to declare conflicts of interest in their published studies, making transparent the motivational factors that can bias the study or its interpretation (Lexchin et al., 2003, Fontanarosa et al., 2005).

[9]Historically, early indications of the harmful effects of BSE, dioxins, and a number of pesticides (EEA, 2001) were reported, but these studies could not compete with mainstream scientific views and the leading opinion makers of the time, and were thus not considered in the regulatory decisions. Yet, there is ample support in the scientific literature that some contested scientists in the minority and dismissed scientific studies have been proven correct. A number of studies claiming undesired effects have also been correctly dismissed, and some studies may yet await acknowledgement or dismissal.

Although it is undisputable that ethical values and bias in data production and interpretation form a core part of scientific knowledge production, the effect thereof is rarely explicitly considered in biological risk assessment or in the public or scientific discourse on how to most efficiently address safety concerns in GE and GMOs. Since it is strongly argued by GMO developers that risk assessment should be 'science-based', a broader consideration of the subjective components of data production is rare. The understanding and identification of the impact of values in biological risk assessment is often confused because the impact occurs at several levels:

> (i) Values shape *knowledge production* by affecting problem framing, hypothesis construction, model choice, experimental design, data interpretation, contextualization, and communication of studies motivated by curiosity-driven data production prior to the applied biosafety context, or studies motivated by the issue or mission-oriented production of safety data supporting the GMO.
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> (ii) Values shape biological *risk assessment* by affecting risk conceptualization, problem framing, data interpretation, evidence weighting, considerations of expert opinions, how poor data quality, conflicting studies or the absence of relevant studies are dealt with, to what extent precautionary-oriented approaches should be taken, and which stakeholders and experts should be a part of the assessment. All these factors will eventually lead to a biased risk communication that is supportive of the risk management plan.
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> (iii) Values shape governmental *risk policy* regarding the laws, liability regime, labelling requirements, and regulatory systems developed for GE and GMOs, the political process determining the composition of, and the design of, the type of decision-making bodies that will conduct the final GMO risk-benefit analysis (of which the biological risk assessment is one of several components), the prioritizing of GE and GMO investment and incentives, and the allocation of resources to biosafety research and broader resource input to curb or shape public opinion. The impact of values in risk assessment and management policies is exemplified by institutional and legislative changes instigated by changes in the political leadership.

Those singly advocating a 'science-based' regulatory system, with the objective of admitting and considering only certain types of data in the risk assessment process, are either deliberately ignorant of the strong influence in the science and regulatory process of the aforementioned exemplified values or have an agenda that benefits from not exposing their own values.[10] The 'science-based' approach can be advocated within a supportive governmental system and a society that share a particular set of values, and hence, they do not necessarily need to be acknowledged as part of the data production and risk assessment process. However, the inherent subjectivity and value component must be explicitly considered and acknowledged when the underlying values supporting the 'science-based' approaches to biosafety are not shared among stakeholders in the global GMO marketplace.

Disagreement between scientists on biosafety issues can be naively explained by pointing to the different 'quality' of the scientists involved. The quality discrepancies may be attributed to the fact that scientists have different overall skills, access to the disputed data, practical knowledge of the methodology, and reach beyond their area of competence, as well as they may apply wrong models, or fail to adequately incorporate related contrasting studies in their contextualization, etc. The construction of the concept of 'sound science' can be seen in this perspective, in which the

[10]They may implicitly advance specific (utilitarian) values that can include limited product regulation and requirements for safety studies, allocation of burden of proof to those voicing safety concerns, decisions to proceed in the face of uncertainty, support for rapid market access of new products, no labelling or liability provisions, broad patent opportunities, corporate control over genetic resources, etc.

concept is used to discredit scientists with opposing views and to claim support for a specific interpretation of the data underlying the safety assessments of GE and GMOs. Thus, the implicit claim of unsound science in some controversial biosafety-relevant studies may often be the result of confusion created by special interests, rather than uniform consensus among independent scientists, representing a broad set of values, on errors in the methodology of a specific study. For example, the study by Quist and Chapela (2001), reporting unexpected introgression of transgenes into corn landraces in Mexico was highly controversial after being published in the leading scientific journal *Nature*.[11] One can speculate as to how many of the peer-reviewed and published, or confidential business information-confined, biosafety studies conducted today follow a quality standard that would stand up to similarly intense and close scrutiny.[12]
The current discourse on the safety of GMOs is taking place within the natural sciences using concepts such as 'science-based', 'sound-science', 'familiarity', and 'substantial equivalence' and is often portrayed as getting the 'right' interpretation of controversial studies. As argued here and elsewhere (Meyer et al., 2005), closer examination of the discourse reveals that subjective assessments, value disagreements, bias, and conflicts of interest define the agendas for the discourse. Thus, disagreement on factual issues can be seen as a strategic discourse adopted to advance and bolster public and regulatory support for the specific objectives of the actors, and discredit those with opposing values and views (Thompson, 2002). Different value sets and risk perceptions direct those scientists who see little uncertainty in GMOs to promote a regulatory-limited, expert-driven, rational, and based-on-available-data-only approach to biosafety. In contrast, those scientists who perceive higher uncertainty and the value-laden context of risk assessment demand more research to fill knowledge gaps, precaution, and individual consumer autonomy and broader stakeholder involvement in the risk analysis.

### *3. Summary*

Biosafety data do not arise from an objective process of data and knowledge accumulation, but represent the scientist's choice of methods and the interpretational context, as determined by the biological, ethical, political, and economic objectives, in which the data is produced. It is important to acknowledge the subjective context underlying all data production, processing, interpretation, and presentation as defined by values, preferences, assumptions, audience, and policies. A transparent handling of these integral components of science and regulatory practice would drastically enhance the quality of data available to regulatory risk assessment and the social robustness of risk analysis while refocusing the ongoing scientific discourse on the safety of GMOs. The future public credibility and trustworthiness of scientists active in the field of

[11]Distinguished scientists, many with strong motivational bias (economic interest in GM plant production) attempted to discredit the study (Christou, 2002). Such unusual peer pressure was made that the Nature editor subsequently wrote that the study should not have been published. Yet, subsequent independent studies conducted by the Government of Mexico confirmed the main observations in the Nature-published study (Alvarez-Morales, 2002), and there is today little scientific controversy over the conclusion that corn transgenes were, at some stage, present in the native corn population of Mexico (Cleveland et al., 2005; Ortiz-Garcia et al., 2005). What remains controversial is the extent to which the transgenes become distributed within the genome of single corn plants. However, this latter aspect is of minor importance to the main observation: that transgenes were present where by law they should not have been. Because the application of all experimental methods requires subjective considerations, any group of influential scientists can discredit the methodology behind most published peer-reviewed studies in any science journal and portray it as 'unsound science'. This exemplifies the science philosopher Bruno Latour's (1987) description of science as an activity where competing knowledge claims are advanced through various networks of scientists, where the stronger network leads the knowledge claim, and competing views struggle for acknowledgement. There have, to our knowledge, been few attempts from those highly vocal in discrediting the Quist and Chapela study to make the Mexican Government publish their three independent studies confirming the presence of transgenes in Mexican corn. If science was an objective unbiased struggle to advance knowledge, should not this be expected?

[12]See also Ioannidis (2005) for an informative discussion on the probability that a research claim is true, taking into account the number of studies conducted, study power, effect size, financial interest and prejudice, bias in model design, data analysis and presentation, and competition in the research field.

biosafety depend on how they identify and acknowledge their objectives and subjective influence on problem framing and choice of methodologies.

Virtually all the broader uncertainties in the science behind GMO safety assessments examined here are not unique to gene technology, but are present in any modern technology assessment. Although this chapter focuses critically on uncertainties, it should not be interpreted as advocating a specific position in disfavour of technological developments in GE and GMOs. Technological advances are always made in the face of uncertainty. Uncertainty is thus not a barrier to scientific progress, but is the main driver of new discoveries, creativity, and inventions. Dogmatic claims assuming 'certainty', rather than uncertainty, stall science (Pollack, 2003). It is the duty of all scientists to identify and challenge the paradigms, values and assumptions shaping their scientific approaches in a reflective and transparent way to ensure that their knowledge claims continually strive for the highest quality.

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