



The EU's GM crop conundrum

Did the EU policy strategy to convert EFSA GMO guidance into legislation deliver on its promises?

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The first genetically modified (GM) crops were introduced more than two decades ago and have been planted globally on more than 190 million hectares (ISAAA, 2020), a surface area larger than all the arable land in the EU. Thousands of risk assessments have consistently concluded that they are as safe as conventional crops in regard to human and animal health (Smyth *et al.*, 2021) and many countries have been growing GM crops for years. Despite political commitments to innovation and investments into research (EC, 2010), the EU is still lagging behind in adopting this technology on a wider scale owing to diverging views among its member states, the European Commission (EC) and the European parliament. Various attempts to resolve this tension by legal and regulatory means have created the most cumbersome and byzantine regulatory system for GM crops in the world. The Implementing Regulation (EU) No 503/2013, meant to ease the regulatory process, has made things even more complicated.

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A major conundrum for the EU is the need to import large quantities of protein-rich

crops such as soybean to supply the continent's livestock industry with high-quality feed.

In the light of the current Russia–Ukraine situation, which has added a layer of instability to already tense markets, the importance of the global agricultural market to ensure food security is even more pronounced.

Given the high adoption rate of GM crops outside the EU, most of these imported commodities inevitably contain GM crops. Under EU law, food and feed products that contain or were produced from GM crops need an import authorisation by the European Commission (EC), which is a lengthy, costly and unpredictable process.

In 2002, the EU set up a centralised review system under Regulation (EC) 178/2002 (the General Food Law Regulation) and an independent scientific body to conduct this review: the European Food Safety Authority (EFSA). EFSA is responsible for performing the risk assessment for food and feed regulated products, including GM crops; their advice “opinion” is used by the EC to draft a decision whether or not to authorise import. EU member states then vote whether or not to follow the EC's draft decision. To date, not a single GM product has received a qualified majority decision for authorisation. The EC then makes the final decision based on EFSA's risk assessment.

There are many reasons why the member states disagree, mostly owing to political and economic agendas. Some members with a large and important agri-food sector tend to vote in line with EFSA's opinions,

while others consistently vote against authorisation or abstain their vote mainly for political reasons. This ongoing disagreement has made it very difficult to establish an EU-wide policy for agricultural biotechnology.

“...the continuous proliferation, update and reinterpretation of EU requirements means that studies that were conducted in compliance with the guidelines at a particular time may no longer comply with changed requirements...”

Implementing Regulation (EU) No 503/2013

To resolve this situation, the EC decided to strengthen the EU regulatory framework for food and feed uses of GM crop products. The intention was to increase member states' trust in EFSA's scientific reviews and risk assessments, so they would have less qualms about voting in line with their opinions. Additional objectives were increasing public trust in the decision-making and providing applicants with clear requirements so as to streamline and shorten the review and approval process. This led to the Implementing Regulation (EU) No 503/2013 in 2013, which incorporated the 2011 EFSA guidance for risk

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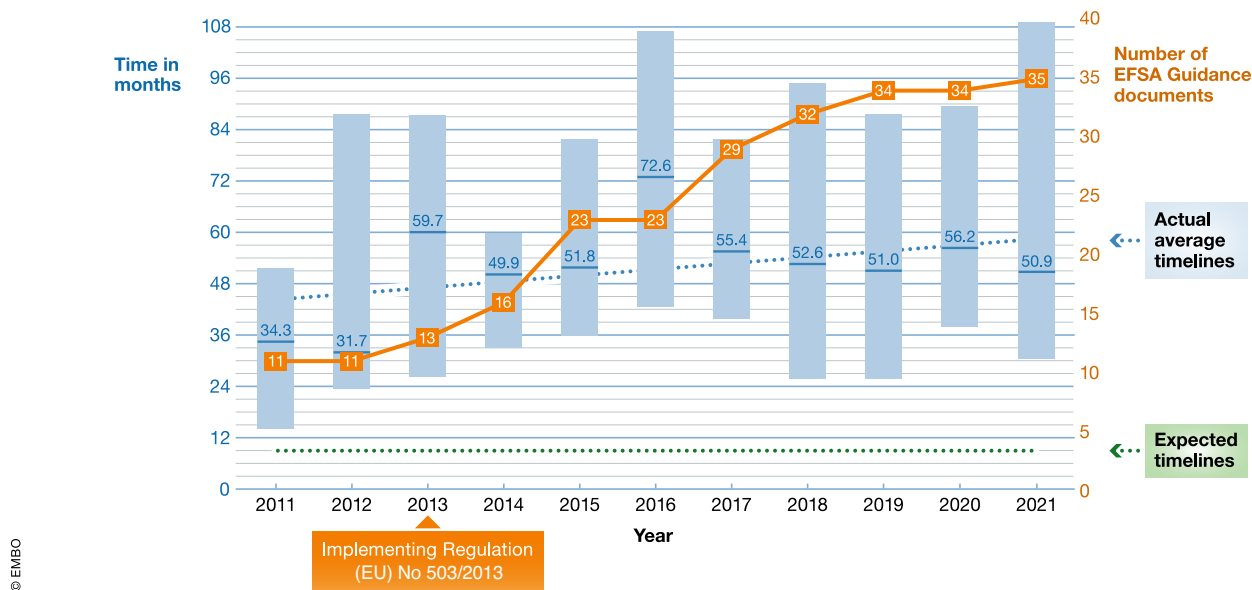


Figure 1. Risk assessment timelines for new GM crop import authorisations in the EU (2011–2021).

Blue bars represent the average (numbers in blue), minimum (lower line) and maximum (upper line) timelines for products finalised within the indicated year. The dotted blue line represents the trend in these average timelines. Line and numbers in orange represent the number of guidelines the notifier needs to consider when submitting a new application. The data was collected from official sources (<https://open.efsa.europa.eu/questions>) and reviewed by CropLife Europe members. Certain cases, with significant delays that may be related to factors beyond the functioning of the risk assessment system, have not been considered to avoid distortions.

assessment of food and feed from GM crops and introduced additional requirements and the legally binding set of evaluation elements and test methods that need to be included in any GM crop application.

The Implementing Regulation has now been in force for more than eight years without meeting its original goal: the Member States’ voting pattern is essentially unchanged, despite the increased data requirements and method harmonisation (EuropaBio, 2017). The Implementing Regulation has also failed to reinforce public trust in the decision-making process or led to a better understanding of the risk analysis framework. It has also failed to achieve its third goal: to streamline and shorten the review process by providing applicants with greater clarity on data requirements and, thus, more predictability of the risk assessment process. Instead, the preparation time for GM crop import applications has increased considerably. While the data requirements imposed by the Regulation might appear to be in line with food and feed safety assessments in other countries, the stipulations for the methods to be used to generate the data essentially require applicants to tailor those studies specifically for the EU. In addition, the continuous proliferation, update and reinterpretation of EU requirements means that studies that were

conducted in compliance with the guidelines at a particular time may no longer comply with changed requirements when new applications for stacked products are reviewed.

As a result, the time that applications take to go through EFSA’s risk assessment is increasing. While the legislation sets a six-month period for finalising EFSA’s opinion, it now takes almost 5 years from submission to finalisation (Fig 1) because there are always several rounds of review that often refer to compliance with method requirements rather than product safety. Products can then take another year to complete the risk management phase, which adds up to almost 6 years from submission to import authorisation. In contrast, the average timeline from submission to authorisation in Australia, Canada, the USA or Brazil is less than two years, even when the scope includes commercial cultivation (Fig 2).

The Implementing Regulation is stifling innovation in the EU

The complex regulatory framework in the EU is challenging but more so for small and mid-size companies. The first challenge is to gain a clear understanding of EU data requirements, as these are continuously updated and reinterpreted (Fig 1). Upon submission

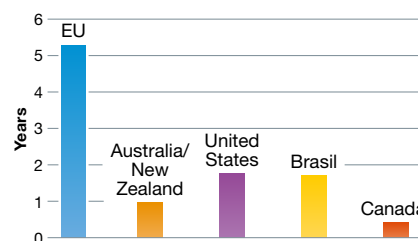


Figure 2. Average time for GM approvals in other regions.

Timelines are based on data from the CropLife International database.

to EFSA, all dossiers are subjected to a completeness check to verify compliance with the latest requirements. New applicants have found this a challenging step, and some applications have taken 15 or more months to pass the completeness check (EFSA, 2019).

Furthermore, industry estimates the cost for GM food and feed approval into the EU between €11 and €16.7 million (EuropaBio, 2019). Many small and mid-size companies and academic institutions simply do not have these resources and cannot justify this financial investment in view of the regulatory uncertainties. In case of cultivation applications and accompanying additional requirements, the investment would be even higher.

This stifles innovation, because GM crops adapted to local conditions that would mainly benefit small producers are not developed. At the same time, the EU has invested in research projects to address important agricultural issues, such as plum trees that are resistant to a virus that is ravaging plum production in some parts of the EU (Petri *et al*, 2018). However, under the current EU system, it is highly unlikely that any of these publicly funded projects will reach the market.

The Implementing Regulation compromises risk assessment approaches

Food safety assessments are based on the identification of hazards and estimations of potential exposure (Fig 3A). Where no hazards are identified, the risk will be minimal regardless of the exposure rate, and *vice versa*.

In most countries, the data submitted to regulatory authorities include a core set of studies and a supplementary set of studies, which are only undertaken if there is a potential harm and, therefore, a testable risk hypothesis (Fig 3B). Key principles in the risk assessment should be case-by-case and weight of evidence, where the data required for the risk assessment of each product depend on the crop/trait combination and the hazards within the scope of the application.

However, the standardisation of data requirements and methods for GM crop import applications enforced by the Implementing Regulation requires an expanded list of mandatory studies, independent of the nature of the crop, the trait and the hazard they may pose. This is limiting the possibility to apply the case-by-case approach, and some of the data requirements are, therefore, unique to the EU (Box 1). Some argue that the Implementing Regulation can accommodate a case-by-case approach as there is a derogation clause that allows applicants to provide scientific reasons for not submitting certain data. In practice, this approach rarely works as EFSA does not accept derogations based on scientific and/or animal welfare grounds for the requirements laid down in the Implementing Regulation.

“... industry estimates the cost for GM food and feed approval into the EU between €11 and €16.7 million.”

Another important difference of the EU system compared with other jurisdictions is the view that combinations of single events by conventional crosses into stacked products generate a new GM plant that needs to go through the full premarket assessment. In contrast, an increasing number of regulatory authorities worldwide are just focusing on the plausible interactions between the events, if any. Regulatory agencies in most countries that allow import and cultivation of GM crops are regularly updating their data requirements for risk assessment based on the experience and history of safe use of GM crops, whereas, in the EU, data requirements continuously increase without a clear rationale. It is important to note that this increase in data requirements is not related to increased safety. The EC, in its assessment of the current framework and its applicability to new genomic techniques, recently acknowledged that the GM legislation does not allow to scale down the requirements based on the safety profile of the product (EC, 2021).

“... the Implementing Regulation has resulted in a complex, unpredictable and costly regulatory system that prevents the use of the case-by-case approach and deviates from basic risk assessment concepts.”

In summary, the Implementing Regulation has resulted in a complex, unpredictable and costly regulatory system that prevents the use of the case-by-case approach and deviates from basic risk assessment concepts. It has not succeeded in changing the voting pattern of member states; it has not increased public acceptance of GM crops nor confidence in the regulatory process. On the contrary, it has created a regulatory system that is difficult to navigate, does not follow basic risk assessment approaches, mandates animal testing for political rather than scientific reasons, which goes against the EU’s own animal welfare legislation (Directive 2010/63/EU) and that overall takes three times longer to approve GM products than in most other countries.

The Implementing Regulation stifles innovation. Its complexity, high cost, time

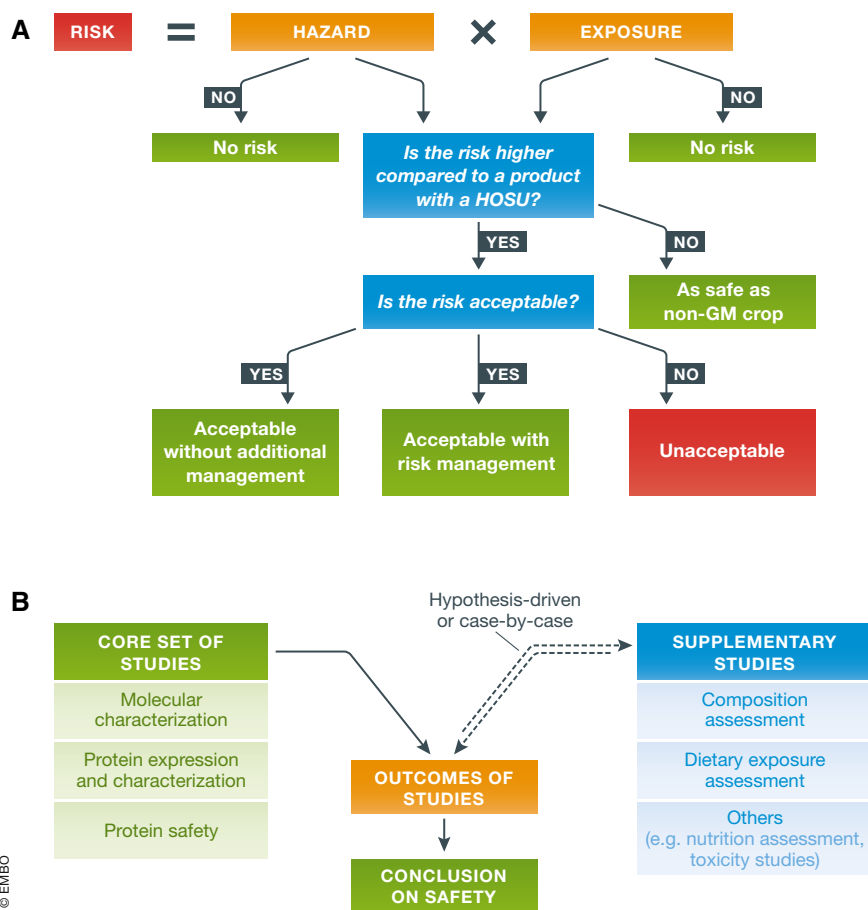
investment and uncertainties with the regulatory requirements limit the number of crops, traits and applicants. GM crop solutions developed for small farmers or for developing countries may, therefore, not be adopted elsewhere, due to concerns that failing to get import authorisation could hamper their exports to the EU (Kalaitzandonakes *et al*, 2015).

Potential improvements to the EU regulatory system

To improve the functionality of the EU regulatory system for GM crops, we propose the following measures.

- Risk managers empower EFSA to complete a case-by-case and proportionate risk assessment within the frame of the Implementing Regulation, which allows derogations based on scientific and technical reasons. This will result in risk assessments based on problem formulation—which takes into account previous experience—with a clear risk hypothesis and data requirements proportional to the risks identified for each product.
- An open dialogue between applicants, EFSA and the EC regarding the scope of the application would facilitate the preparation of fit-for-purpose applications and improve the efficiency of the assessment. Similarly, open and science-based discussions on issues encountered during the risk assessment would facilitate a common understanding and efficient resolution.
- Ensuring that animal feeding trials are scientifically warranted and compliant with the Directive 2010/63/EU on the protection of animals used for scientific purposes. A similar system as set up by the European Chemical Agency could be established at EFSA.
- Strengthened risk communication by the European Commission and the EU Member States.
- Aligning with other countries on the regulation of GM stacked products obtained through conventional breeding and focusing only on products where interactions between the traits pose a potential hazard.

Adopting these recommendations would increase the predictability of the EU regulatory system for GM crops without jeopardising safety standards and may help to foster innovation by encouraging



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Figure 3. Risk assessment principles and overview of the studies necessary to assess food and feed safety.

Panel A describes the components of risk assessment and their application in decision-making. Panel B represents the recommendations for science-based food and feed risk assessments for GM crops (Waters *et al*, 2021) (HOSU: history of safe use).

Box 1. Example of requirements not based on science

According to the Implementing Regulation, all single GM product applications for import must contain a 90-day rat feeding study. This was included in the Implementing Regulation against the advice of EFSA (Waigmann *et al*, 2013; Devos *et al*, 2016) who argued that these feeding studies should only be performed on a case-by-case basis when a hazard was identified and with a clear risk hypothesis. The EC was legally bound to review this requirement considering the results of the EU-funded research projects: GRACE and G-TWYST, which concluded that “we do not see the need to continue with the mandatory requirement to conduct untargeted animal feeding studies for each novel GM plant” (G-TWYST & GRACE, 2018). Despite this evidence, the EC has maintained the requirement for these 90-day feeding studies. And while EFSA did not support the mandatory nature of this requirement, compliance is now enforced and guidelines on how the studies should be conducted have been published. In some cases, when developers submit applications for the approval of stacked GM products, they face the situation that the animal feeding studies that were formerly conducted and accepted in the assessment for single events are rejected as they do not meet the new method requirements. EFSA has so far not accepted derogation requests to avoid the need for additional animal sacrifice as is the aim of the EU’s animal welfare legislation (Directive 2010/63/EU). This also goes against the principle of weight of evidence whereby small shortcomings should not lead to the overall rejection of a study.

applications from other developers such as smaller companies or academia.

In conclusion, what was perceived by EU regulators as a potential solution to resolve the stalemate with GM food and feed imports has backfired and made the regulatory framework even more complex, lengthy and cumbersome. If the EU is to fulfil its promises of creating an innovation-based economy along with sustainable agriculture and food safety, the regulatory process for current GM crops and future agricultural biotechnology developments needs to be made proportionate.

Disclosure and competing interests statement

Petra Kostolaniova is an employee of CropLife Europe, the European association that represents sustainable crop protection solutions in the area of pesticides and biopesticides, digital and precision farming and plant biotechnology innovation. Mònica García-Alonso is an independent consultant and director of Estel Consult Ltd that provides ad hoc technical support to the plant biotechnology sector of CropLife Europe under a consultancy contract. Concepción Novillo is an employee of Bayer CropScience. Maica Martínez Parrilla is an employee of BASF. Esteban Alcalde is an employee of Syngenta. Nancy Podevin is an employee of Corteva Agriscience. They are members of CropLife Europe expert groups and employees of companies involved in the development and marketing of agricultural inputs, including GM crops, with a financial interest in the subject matter.

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