

# Comparative Analysis of Risk Assessment Procedures for Genetically Modified Crops in the European Union and the United States

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# **ABSTRACT**



The US has approved several new biotech fruits, such as non-browning Arctic® Apples, Pink-Fleshed 'Rosé' Pineapples, and Cotton Candy® grapes, while the EU is still struggling to allow primary GM crops to enter their market. GM crops are biotechnological innovations that hold great potential future benefits in overcoming the challenges of increasing food crop production and ensuring global food security. To reap the benefits of these applications, the producer must participate in a risk assessment procedure before the GM products can be approved for the market. This is a crucial step to evaluate possible adverse effects of bioengineered crops that may represent a threat to the health of humans and animals or bring negative environmental impacts. The EU and US are the leading countries in biotech innovation, but they often take a different approach in handling GMOs. In most cases, the US biotech companies are the producers, while the European Food Safety Authority (EFSA) in the EU will act as a risk assessor, even though the GM crops from the US have gone through a comprehensive safety assessment in their home country, which acts as the first process of risk assessment. There is a gap in knowledge between the risk assessment procedures that have been done in the EU and the US, and they are often motivated by different rationales. To illuminate this problem, this paper will investigate the regulatory framework for the risk assessment of GM crops in both countries from the comparative legal perspective.

**KEY WORDS:** Comparative analysis, Genetically Modified (GM) Crops, GM risk assessment, GM labelling, GM legislation in the EU, GM legislation in the US

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# LIST OF ABBREVIATION



APHIS Animal and Plant Health Inspection Service

AMS Agricultural Marketing Service

BT Bacillus thuringiensis

BE bioengineered

Biotechnology WG Biotechnology Working Group

BRS Biotechnology Regulations Services

CA Competent Authority

CBI confidential business information

CFR Code of Federal Regulations

CFS Center for Food Safety

CFSAN Center for Food Safety and Applied Nutrition

CPB Cartagena Protocol on Biosafety

CRISPR Clustered Regularly Interspaced Short Palindromic Repeats

CVM Center for Veterinary Medicine

DOI Declarations of Interests
EC European Commission

ECJ The Court of Justice of the European Union

EFSA European Food Safety Authority
EIS environmental impact statement
EPA Environmental Protection Agency

e.r.a environmental risk assessment

EU European Union

EUP experimental use permit FBOs food business operators

FDA Food and Drug Administration

FD&C Federal Food, Drug, and Cosmetic Act

FIFRA Federal Insecticide, Fungicide, and Rodenticide Act

FOIA Freedom of Information Act

FTO Freedom to Operate

FSIS Food Safety and Inspection Service

GM Genetically modified
GE genetic engineering

GMO Genetically modified organism

GRAS Generally Recognized as Safe

MS Member States

NBFS national bioengineered food standard
NEPA National Environmental Policy Act

NOI notice of intent

NTOs non-target organisms

NPBTs new plant breeding techniques
OPP Office of Pesticide Programs

PAD Public Access Document

PPA Plant Protection Act

PPRA Plant Pest Risk Assessment
PAD Public Access to Documents

RA Risk Assessment

RRA Roundup Ready alfalfa

RRSB Roundup Ready sugar beets

SMEs Small and medium-sized enterprises

TALENs Transcription activator-like effector nucleases

US United States

USDA United States Department of Agriculture



### 1.1 RESEARCH BACKGROUND

The world's population is estimated to reach 9.8 billion people by the year 2050. This will cause an immense increase in the demand for food and animal feed, requiring production to increase by 70% in order to ensure global food and nutrition security. It is estimated that the degradation of natural resources will slow the rate of increase in future crops. Some scientists have even claimed that the current farming system has reached its maximum capacity, and therefore an increase in agricultural innovation should become a priority. Without greater innovation, the responsibility to feed the world's population will be a daunting task.

To overcome this problem, biotech scientists are rising to the challenge by offering solutions based in the agricultural use of scientific tools and techniques. Advancements in genetic engineering techniques such as CRISPR and TALENs have become indispensable tools in improving plant traits and varieties in ways that can lead to better yields, more resilience, and greater profits through reductions in the usage of insecticide in the fields.<sup>5</sup> Furthermore, manipulating crops may also enhance the quantity and quality of nutrients in the crops to levels that may not exist naturally or that may be lacking. Two examples are "golden rice," which contains provitamin A to prevent blindness in children,<sup>6</sup> and GM cassava, which has more protein to reduce malnutrition.<sup>7</sup> GM crops are currently dominated by cotton, maize, and soybean varieties. By the year 2020, however, it is estimated that more specialty crops, such as bean and sugarcane, will start to be commercialized.<sup>8</sup>

Before entering the market or starting cultivation, the producers of GM agricultural products must prove not only that their products pose no threats to the environment, but also that their products do not pose any adverse effects that may threaten the health of humans or animals. This process is called a risk assessment. These are based on science and vary from country to country. As the leading

<sup>4</sup> Mulhollem, J. (2017). *Widely accepted vision for agriculture may be inaccurate, misleading*. Retrieved October 12, 2018, from <a href="https://news.psu.edu/story/452218/2017/02/22/widely-accepted-vision-agriculture-may-be-inaccurate-misleading">https://news.psu.edu/story/452218/2017/02/22/widely-accepted-vision-agriculture-may-be-inaccurate-misleading</a>

<sup>&</sup>lt;sup>1</sup> UN. (2017). *World population projected to reach 9.8 billion in 2050, and 11.2 billion in 2100*. Retrieved October 12, 2018, from <a href="https://www.un.org/development/desa/en/news/population/world-population-prospects-2017.html">https://www.un.org/development/desa/en/news/population/world-population-prospects-2017.html</a>

 $<sup>^2</sup>$  FAO. (2009).  $Global\ agriculture\ towards\ 2050.$  Retrieved October 12, 2018, from  $\underline{\text{http://www.fao.org/fileadmin/templates/wsfs/docs/Issues\_papers/HLEF2050\_Global\_Agriculture.pdf}$ 

<sup>&</sup>lt;sup>3</sup> Ibid

<sup>&</sup>lt;sup>5</sup> Matthew, J., Michael, L., & Sankar, S. (2017). Are GM crops for yield and resilience possible? *Trends in plant science*.

<sup>&</sup>lt;sup>6</sup> Potrykus, I. (2001). Golden rice and beyond. *Plant physiology*, 125(3), 1157-1161.

<sup>&</sup>lt;sup>7</sup> Stupak, M., Vanderschuren, H., Gruissem, W., & Zhang, P. (2006). Biotechnological approaches to cassava protein improvement. *Trends in food science & technology*, *17*(12), 634-641.

<sup>&</sup>lt;sup>8</sup> Parisi, C., Tillie, P., & Rodríguez-Cerezo, E. (2016). The global pipeline of GM crops out to 2020. *Nature biotechnology*, *34*(1), 31.

countries in the development of food safety systems,<sup>9</sup> the EU and the US employ highly developed risk assessment procedures. The US so far has approved 202 GM crops varieties,<sup>10</sup> which are not only produced for domestic use but also exported to many countries, including to the EU. Furthermore, the US is the largest GM exporter and producer, having cultivated around 75 million hectares of GM crops worth \$80.3 billion.<sup>11</sup> This has established the US as the most important risk assessor for GMOs appearing in international trade.<sup>12</sup> The EU has imported an enormous amount of soybean and soymeal as feedstuff, and a limited amount of GM food, from Brazil, Argentina, and the US.<sup>13</sup> Regardless of the fact that the imported GM products have already passed the risk assessment process in their countries of origin, these products must also pass another approval procedure in the EU by submitting application dossiers to the appropriate Competent Authority (CA) for evaluation by EFSA. This complicated procedure may have negative effects on the development of biotech innovation inside the EU. It is also possible that some of the great inventions in genetic engineering (GE) that originate in non-EU countries may not reach the EU market because their owners lose interest.<sup>14</sup> The lengthy and costly approval procedure for GM crops may limit its international market.<sup>15</sup>

# 1.2 PROBLEM DEFINITION

There is a gap in knowledge between the risk assessment procedures that have been done in the EU and the US, and they are often motivated by different rationales. Several scholars have argued that the US risk assessment system is predominantly based on product <sup>16</sup> and the EU is focused on the process <sup>17</sup>, but other and more precise distinctions are still unknown. These would include, for example, the kind of dossiers or the procedural steps that might be different.

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<sup>&</sup>lt;sup>9</sup> Spiric, D., Jovanovic, D. R., Palibrk, V. P., Bijelovic, S., Djuragic, O., & Reddy, P. G. (2015). Convergence on EU and USA Food Safety Regulation approach, regarding foodborne outbreaks. *Procedia Food Science*, 5, 266-269.

<sup>&</sup>lt;sup>10</sup> ISAAA. (2018). *GM Crop Events approved in United States of America*. Retrieved September 17, 2018 from <a href="http://www.isaaa.org/gmapprovaldatabase/approvedeventsin/default.asp?CountryID=US&Country=United%20States%20of%20America">http://www.isaaa.org/gmapprovaldatabase/approvedeventsin/default.asp?CountryID=US&Country=United%20States%20of%20America</a>

<sup>&</sup>lt;sup>11</sup> ISAAA. (2017). Global Status of Commercialized Biotech/GM Crops in 2017: Biotech Crop Adoption Surges as Economic Benefits Accumulate in 22 Years. Retrieved October 12, 2018, from <a href="http://www.isaaa.org/resources/publications/briefs/53/download/isaaa-brief-53-2017.pdf">http://www.isaaa.org/resources/publications/briefs/53/download/isaaa-brief-53-2017.pdf</a>

Peck, Alison, Leveling the Playing Field in GMO Risk Assessment: Importers, Exporters and the Limits of Science (March 11, 2011). Boston University International Law Journal, Vol. 28, No. 2, 2010. Available at SSRN: <a href="https://ssrn.com/abstract=1783865">https://ssrn.com/abstract=1783865</a>

<sup>&</sup>lt;sup>13</sup> European Commission. (2015). *Fact Sheet: Questions and Answers on EU's policies on GMOs*. Retrieved September 17, 2018 from <a href="http://europa.eu/rapid/press-release\_MEMO-15-4778\_en.htm">http://europa.eu/rapid/press-release\_MEMO-15-4778\_en.htm</a>

<sup>&</sup>lt;sup>14</sup> Bradford, K., Carter, N., Eriksson, D., Grabau, E., Hood, E., Parrott, W., & Wolt, J. D. (2018). Regulatory barriers to the development of innovative agricultural biotechnology by small businesses and universities. *Issue Paper-Council for Agricultural Science and Technology*, (59)

<sup>&</sup>lt;sup>15</sup> Grossman, M.R. (2018). Agricultural Biotechnology: Regulation in the United States and the European Union p.365. In: *Regulating and managing food safety in the EU: A legal-economic perspective*. Bremmers, H and Purnhagen, K (ed). Economic analysis of law in European legal scholarship, volume 6. Cham, Switzerland: Springer.

<sup>&</sup>lt;sup>16</sup> Sprink, T., Eriksson, D., Schiemann, J., & Hartung, F. (2016). Regulatory hurdles for genome editing: process-vs. product-based approaches in different regulatory contexts. *Plant cell reports*, *35*(7), 1493-1506.

<sup>&</sup>lt;sup>17</sup> Marchant, G. E., & Stevens, Y. A. (2015). A new window of opportunity to reject process-based biotechnology regulation. *GM crops & food*, *6*(4), 233-242.

#### 1.3 RESEARCH OBJECTIVE

This thesis will investigate the regulatory frameworks for GM crop risk assessment both in the EU and the US and identify their differences. The next objective is to analyse the factors that may cause the differences between the risk assessment procedures in those countries. The EU and US are selected because they are the first and foremost practitioners in the area of food safety regulation as it relates to GMOs. Additionally, most of the risk assessment processes in the EU and the US are conducted transparently, and therefore provide sufficient information to be analysed.

# 1.4 RESEARCH QUESTION

With the intention of accomplishing the research objective, the following research questions will be investigated:

- 1. What are the **differences** in the GM crop risk assessment procedures of the EU and the US?
- 2. What are the **factors causing the differences** in GM crop risk assessment procedures in the EU and the US?

# 1.5 METHODOLOGY

The research for this thesis applies comparative legal analysis using an analytical approach to distinguish differences and commonalities between the legal systems <sup>18</sup>. This method is used while delving into the EU and the US legal system related to GMOs using primary sources as follows:

- Regulation (EC) 1829/2003 on genetically modified food and feed;
- Directive 2001/18/EC on the deliberate release of GMOs into the environment;
- Directive (EU) 2015/412 amending Directive 2001/18/EC as regards the power of the Member States to restrict or prohibit the cultivation of GMOs in their territory;
- Regulation (EC) 1830/2003 concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms;
- Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28
  January 2002 laying down the general principles and requirements of food law,
  establishing the European Food Safety Authority, and putting in place procedures in
  matters of food safety;
- Commission Implementing Regulation (EU) No 503/2013 of 3 April 2013 on applications for the authorisation of genetically modified food and feed;

<sup>&</sup>lt;sup>18</sup> Van Hoecke, M. (2015) Methodology of comparative legal research. *LAW AND METHOD*. Boom: Boom Juridische Uitgevers; 1–35. MLA. <a href="https://doi.org/10.5553/rem/.000010">https://doi.org/10.5553/rem/.000010</a>

- Commission Directive (EU) 2018/350 of 8 March 2018 amending Directive 2001/18/EC
  of the European Parliament and of the Council as regards the environmental risk
  assessment of genetically modified organisms
- Plant Protection Act (PPA);
- Federal Food Drug and Cosmetic Act (FFDCA);
- Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

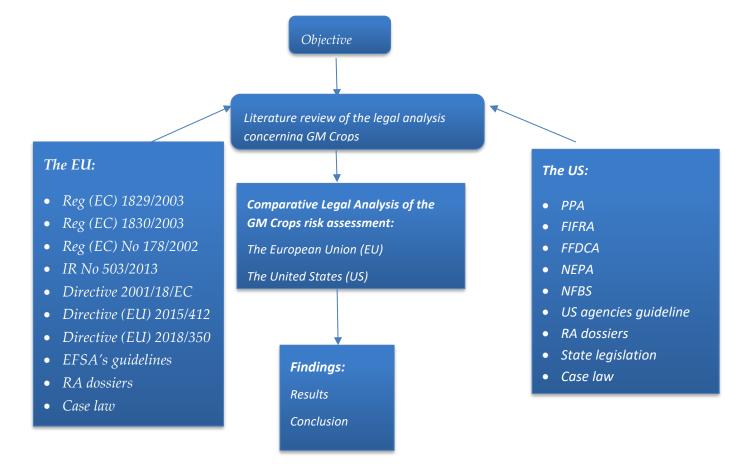


Figure 1.6 Research Framework

The secondary sources include guidelines from EFSA and US agencies; case law; EFSA's scientific opinions; the risk assessment dossier submitted by the applicant; and the other supporting documents related to the GMOs. Furthermore, a review of the literature in scientific journals that contains the ideas of other legal scholars on the subject will also be taken into account. Note, however, that this thesis will not elucidate all the details of the legislation and the documents but will rather focus on particular aspects that are of interest in answering the research questions. Besides, this thesis will exclude the regulation of GM microorganisms and their products, because the EU and the US have regulated these separately from GM crops. The definition of crops used herein is in accordance with that of the FAO, with the scope covering crops such as cereals, vegetables, fruits and nuts, oilseed

crops, tubers, legumes, sugar crops, and other common crops (cotton, tobacco, etc.).<sup>19</sup> This thesis will only discuss those GM crops that are intended to function as food or feed, or are intended for other agricultural practices.

To understand the risk assessment in practice, it is necessary to obtain the original documents submitted by the applicants. Thus, several Freedom of Information Act (FOIA) requests have been made to the FDA, APHIS-USDA, and EPA. In the EU, the Public Access Documents (PAD) facilitate the public to get the access to the documents which are not available on the EU institutions websites in accordance with transparency policy<sup>20</sup> and right of access<sup>21</sup> enacted in the EU. During this thesis period, PAD has been requested to EFSA, as the EU risk assessor for GMOs.

# 1.6 RESEARCH FRAMEWORK

The research steps are depicted in Figure 1.6. This thesis is divided into four chapters. The first chapter is the introduction which explains the research background, the methodology, and the research question. The second chapter will provide the legal analysis for GM crops in the EU and the US. The third chapter will focus on presenting the results of a comparative analysis between the two countries. The fourth chapter will draw conclusions which will provide the answers to the research questions and offer recommendations for further research.

<sup>&</sup>lt;sup>19</sup> FAO. (2015). A System of Integrated Agricultural Censuses and Surveys, p: 144-146. Rome: FAO

<sup>&</sup>lt;sup>20</sup> Recital 3 of Regulation (EC) No 1049/2001

<sup>&</sup>lt;sup>21</sup> Art 2(1) Regulation (EC) No 1049/2001



#### 2.1 INTRODUCTION

GMO regulations for both the EU and the US are established as inert monoliths, which have not significantly changed since the first introduction of GMOs. More recently, however, the Court of Justice of the European Union (ECJ) in Luxembourg has made a breath-taking decision, holding that modern gene editing techniques, including CRISPR-Cas 9 and other modern mutagenesis techniques, are to be subjected to GM regulations.<sup>22</sup> This means that every gene-edited crop, even one that does not contain any recombinant DNA, must follow the GM authorization procedure as well as meeting the labelling and traceability requirements.

In the US, meanwhile, the update of Coordinated Federal Framework for the Regulation of Biotechnology in 2017 has brought several changes, especially concerning the roles of federal agencies. One important change allows the exemption of a battery of new plant breeding techniques (NPBTs). These will not be bound by regulatory oversight upon the condition that they were not produced using plant pests, nor fall into the category of plant pests.<sup>23</sup> This situation has given rise to new opportunities for researchers in the US who wish to continue their research on plant breeding innovation. It will also encourage small and medium-sized enterprises (SMEs) to develop and market their innovations. In 1994, the first engineered tomato, better known as FLAVR SAVR tomato produced by Calgene, Inc., was successfully introduced in the US market. It was eventually withdrawn in 1997 due to the high cost of production.<sup>24</sup> Recently, Cellectis Plant Sciences Inc., which has transformed into Calyxt, Inc., has been using TALENs to enhance some soybean varieties, resulting in a better quality of fatty oil acid.<sup>25</sup> Other innovative products such as Arctic® Apple, Del Monte Rose Pineapple, and Innate® Potato have been successfully introduced to the US market, providing better quality and larger choices to meet consumers preferences. These examples offer a brief illustration of how the gene edited crops regulatory framework—in practice—is conducted in a dissimilar fashion. The in-depth explanation related to the GMO regulatory framework in both countries will be depicted in the next part of this chapter.

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<sup>&</sup>lt;sup>22</sup> Judgement of 25 July 2018, Confédération paysanne and Others v Premier ministre, Ministre de l'Agriculture, de l'Agroalimentaire et de la Forêt, ECLI:EU:C:2018:583

<sup>&</sup>lt;sup>23</sup> USDA. (2018). Secretary Perdue Issues USDA Statement on Plant Breeding Innovation. Retrieved September 21, 2018 from <a href="https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation">https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation</a>

<sup>&</sup>lt;sup>24</sup> Bruening G, Lyons J. 2000. The case of the FLAVR SAVR tomato. *Calif Agr* 54(4):6-7.

<sup>&</sup>lt;sup>25</sup> Haun, W., Coffman, A., Clasen, B. M., Demorest, Z. L., Lowy, A., Ray, E., ... & Mathis, L. (2014). Improved soybean oil quality by targeted mutagenesis of the fatty acid desaturase 2 gene family. *Plant biotechnology journal*, 12(7), 934-940.

#### 2.2 THE EUROPEAN UNION LEGAL SYSTEM WITH REGARD TO GM REGULATION

# 2.2.1 AN OVERVIEW OF THE EUROPEAN UNION INSTITUTIONAL BACKGROUND GOVERNING GMOS

The concept of multigovernance concerning GMOs in the EU is dominated by political nuance in the dispersal of authority and the slow progress of decision making,<sup>26</sup> and the process of risk assessment tries to minimize the political element.<sup>27</sup> In general, there are various institutions which are embroiled in the risk analysis of GMOs in the EU as described below:

In the very beginning, several panel experts selected by EFSA, along with a number of external scientists, shared the main task of evaluating the applicant's dossiers during the process of risk assessment. The dossiers had been submitted by the CA from MS where the applicant had first applied. The principles of science, conducted transparently and objectively, underly the EFSA's risk assessment as an EU independent body.<sup>28</sup> These panels have a thorough knowledge of food and feed safety assessment, environmental risk assessment (e.r.a), and molecular characterisation in plant science.<sup>29</sup> Before and after each meeting, forms called Declarations of Interests (DOI) must be filled by the meeting members to ensure that no conflicts of interests exist with the applicant (e.g the biotech company); if any are found, those members will not be able to join the meeting.<sup>30</sup> To support this process, particularly the authentication of the GM detection methods, the Community reference laboratory will be tasked as explained in the Annex of the Regulation (EC) No 1829/2003, for which the operating cost will be partly paid by the producers.<sup>31</sup> Next, the European Commission (EC), as a risk manager, will document the results of the risk assessment and render a final decision. Throughout this process, the EFSA, the EC, and MS shall collaborate to assure that every measure is conducted accordingly.<sup>32</sup>

Besides the EU Institutions that have been mentioned above, in 2010, EFSA established "the GMO network," which is comprised of the organisations from the Members States (MS) as the core members. The non EU organisations are included as observers.<sup>33</sup> A meeting is held once every year to share the best practices of GM risk assessment and to provide valuable input for EFSA. This is done to

<sup>&</sup>lt;sup>26</sup> Lee, M. (2010). Multi-level governance of Genetically Modified Organisms in the European Union: Ambiguity and Hierarchy p.100-102. In: *The regulation of genetically modified organisms: Comparative approaches.* Bodiguel, L., Jurist., & Cardwell, M (ed). Oxford: Oxford University Press.

<sup>&</sup>lt;sup>27</sup> Morrow, K. (2010). Genetically Modified Organisms and Risk, p.57. In: *The regulation of genetically modified organisms: Comparative approaches*. Bodiguel, L., Jurist., & Cardwell, M (ed). Oxford: Oxford University Press.

<sup>&</sup>lt;sup>28</sup> Art 6(2) Regulation (EC) No 178/2002

<sup>&</sup>lt;sup>29</sup> EFSA. (2018). *Panel on Genetically Modified Organisms*. Retrieved September 21, 2018 from <a href="https://www.efsa.europa.eu/en/panels/gmo">https://www.efsa.europa.eu/en/panels/gmo</a>

<sup>&</sup>lt;sup>30</sup> DOI and CV of panels can be accessed publicly at <a href="https://ess.efsa.europa.eu/doi/doiweb/doisearch/panel/GMO/wg/684410">https://ess.efsa.europa.eu/doi/doiweb/doisearch/panel/GMO/wg/684410</a>

<sup>31</sup> Art 32 Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>32</sup> Art 22(8) Regulation (EC) No 178/2002

<sup>&</sup>lt;sup>33</sup> List of the GMO network members available at <a href="https://www.efsa.europa.eu/sites/default/files/assets/gmonetworklist.pdf">https://www.efsa.europa.eu/sites/default/files/assets/gmonetworklist.pdf</a>

enhance the harmonisation between the MS. In sum, the science itself can not provide a conclusive answer to the risks posed by GMOs. A regulatory framework is needed to view this topic from a definitive perspective.

# 2.2.2 THE EUROPEAN UNION LEGAL FRAMEWORK ON GMO CROPS

The provisions regulating GMOs are layed down in the EU regulatory framework, which is divided into regulations, directives, decisions, recommendations, and opinions. The first three are binding legislative acts, while the last two are nonbinding.<sup>34</sup> However, a recommendation which appears under another name, such as a guideline, may have a binding effect on the issuing organization since it contains concerned views and suggestions. In these cases, the EFSA's guidelines provide detailed information addressed to the companies about the GM authorization process along with important scientific guidance that was not covered by regulations or directives. These guidelines are often created after consultation with the industry to confirm their feasibility<sup>35</sup> in order to persuade them to comply with the requirements. The companies themselves have great incentive to follow these guidelines in order to avoid liability issues that may result from any noncompliance with recommended guidelines. These guidelines are often stated in the regulations. The EFSA's guideline for the implementation of part C of Annex of Directive 2001/18/EC is a good example. The GM guidance created by EFSA was based upon the opinion from the EC, along with information taken from CODEX, OECD, JRC, EMA, ECDC, and biosafety research.<sup>36</sup> Thereby, the role of EFSA's guidelines is significant in the step of risk assessment.

Moving on now to consider about the GMOs. A GMO is defined as "an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination" (Art 2(2) Directive 2001/18/EC). The GMO must have been created as a result of at least one of these techniques: recombination of nucleic acids; transferring heritable material from the outside of organism; and cell fusion or hybridisation (Annex I A, part 1 of Directive 2001/18/EC). Pursuant to Art 2(2b) Directive 2001/18/EC, "the techniques of in vitro fertilisation; natural processes (conjugation, transduction, transformation); and polyploidy induction;" are exempt and are not considered as GMOs to be listed in Annex I A, part 2. Furthermore, as referred to in Article 3 (1) of this Directive, mutagenesis and cell fusion, as they are listed in Annex I B, are also included in the exemption. There has been a debate for several years regarding the term mutagenesis and whether new plant breeding techniques are part of it. On 25 July 2018, the ECJ

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<sup>&</sup>lt;sup>34</sup> Article 288 Treaty on the Functioning of the European Union (TFEU)

<sup>&</sup>lt;sup>35</sup> Corporate Europe. (2012). *Conflicts on the menu*. Retrieved September 22, 2018 from https://corporateeurope.org/sites/default/files/publications/conflicts\_on\_the\_menu\_final\_0.pdf

<sup>&</sup>lt;sup>36</sup> EFSA. (2016). EFSA Organization & Procedures for GMO Risk Assessment EFSA Organization & Procedures for GMO Risk Assessment Yi Liu Scientific officer Taiex workshop. Retrieved September 26, 2018 from https://slideplayer.com/slide/10154759/

decided that modern breeding techniques will be subjected to the GMO regulation.<sup>37</sup> This brought great disappointment to many parties, especially among the biotech companies and NPBT researchers who lost their incentive to nurture these technologies.<sup>38</sup> Bayer, BASF, KWS,<sup>39</sup> and HZPC<sup>40</sup> are among the plant breeding companies in Europe that have announced plans to move their research departments to the US as a response to this strict ruling.

Pursuant to the precautionary principle, the EU has promulgated Regulation (EC) No 1829/2003, which established procedures for the authorization, supervision, and labelling of food and feed. Further, Art 4(1) underlined that GMOs used for food should not: "(a) have adverse effects on human health, animal health or the environment; (b) mislead the consumer; (c) differ from the food that would be nutritionally disadvantageous for the consumer."

This was followed by the next Art 4(2), which stated that GM foods could not be placed on the market without having undergone the authorisation process, unless the products contain no more than 0.5% of GMOs with the following conditions that the "this presence is adventitious or technically unavoidable ", the material has received a positive opinion prior to this Regulation, the GM application has never been rejected, and there is a public access to the methods to detect this presence.<sup>41</sup> Nonetheless, the producers must also prove that they have taken the necessary steps to prevent the adventitious presence of the GMO in other products.<sup>42</sup>

In the EU, the applicant can apply for the approval procedure for GMOs depending on the purpose or lack thereof, in other words, whether it is for food and feed, or cultivation, or both. The latter one is referred to as the "one door, one key principle" which is often avoided by applicants considering the risk of a full rejection. <sup>43</sup> The application for cultivation is much more stringent, and currently there are only few of GM crops that have been granted authorization. Two renowned examples are Mon 810 maize, which was approved for cultivation in 1998, and Amflora starch potato (EH92-527-1), approved in 2010. The Amflora starch potato authorization decision, however, was annulled in 2013 by the General Court, <sup>44</sup> which leaves Mon 810 Maize as the only GM crop that has been approved for cultivation for the time being. Another application for cultivation, that of maize 5912, has been

<sup>&</sup>lt;sup>37</sup> Judgement of 25 July 2018, Confédération paysanne and Others v Premier ministre, Ministre de l'Agriculture, de l'Agroalimentaire et de la Forêt, ECLI :EU:C:2018:583

<sup>&</sup>lt;sup>38</sup> Callaway, E. (2018). CRISPR plants now subject to tough GM laws in European Union. *Nature*, 560(7716), 16.

<sup>&</sup>lt;sup>39</sup> Burger. L. (2018). *Bayer, BASF to pursue plant gene editing elsewhere after EU ruling*. Retrieved October 30, 2018 from <a href="https://www.reuters.com/article/us-eu-court-gmo-companies/bayer-basf-to-pursue-plant-gene-editing-elsewhere-after-eu-ruling-idUSKBN1KH1NF">https://www.reuters.com/article/us-eu-court-gmo-companies/bayer-basf-to-pursue-plant-gene-editing-elsewhere-after-eu-ruling-idUSKBN1KH1NF</a>

<sup>&</sup>lt;sup>40</sup> Engwerda, J. (2018). *HZPC gaat gen-onderzoek buiten EU doen*. Retrieved October 30, 2018 from <a href="https://www.boerderij.nl/Akkerbouw/Achtergrond/2018/7/HZPC-gaat-gen-onderzoek-buiten-EU-doen-314723E/">https://www.boerderij.nl/Akkerbouw/Achtergrond/2018/7/HZPC-gaat-gen-onderzoek-buiten-EU-doen-314723E/</a>

<sup>&</sup>lt;sup>41</sup> Art 47(1) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>42</sup> Art 47(2) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>43</sup> Meulen, B. V. D., & Yusuf, N. (2015). One-door-one-key principle: observations regarding integration of GM authorization procedures in the EU. *Penn St. L. Rev.*, 118, 877.

<sup>&</sup>lt;sup>44</sup> Judgement of 13 December 2013, *Hungary v European Commission*, Case T-240/10

rejected. The reason for the rejection was the uncertainty of the potential risk to the environment, specifically the effects on honeybee and ladybird populations.<sup>45</sup>

It is important to note that the MS now have the freedom to choose either to approve or to ban the cultivation of GMOs in their territories. In accordance with Art 1 Directive (EU) 2015/412, since 3 April 2017, any MS which approves the cultivation would bear the full responsibility to prevent any cross border contamination to another MS which has rejected the cultivation of GM crops.

# 2.2.3 RISK ASSESSMENT PROCEDURE OF GM CROPS

The risk assessment of GM crops is a crucial step designed to evaluate the adverse effects of GM plants. The process of risk assessment is defined under Art 3(11) Regulation (EC) No 178/2002 as, "a scientifically based process consisting of four steps: hazard identification, hazard characterisation, exposure assessment, and risk characterisation." The goal is to protect the safety and health of humans and animals, together with the preservation of the environment. Risk assessment is part of the risk analysis process, which consists of risk analysis, risk management, and risk communication, with all three components being one coordinated process. In the EU, EFSA (scientists) will act as the risk assessor, while the EC serves as the risk manager, however, this thesis will only focus on the risk assessment procedure, without addressing the two other processes. The process of risk assessment, as illustrated in **Figure 2.1**, is started when the company submits dossiers from the applicant to the Competent Authorities (CA) in the MS with the following information (**Table 2.2.3**).

Table 2.2.3 List of information for the submission to the Competent Authorities (CA) based on Art 5(3) Regulation (EC)No 1829/2003

Type of Info	Details	
Applicant information	Name and address	
Product information	The designation of the food, and its specification, including the transformation event(s) used	
Cartagena Protocol on Biosafety to the Convention on Biological Diversity*		
Production method*	A detailed description of the method of production and	

<sup>&</sup>lt;sup>45</sup> EFSA. (2013). Statement supplementing the environmental risk assessment conclusions and risk management recommendations on genetically modified insect-resistant maize 59122 for cultivation in the light of new scientific information on non-target organisms and regionally sensitive areas. *EFSA Journal*;11(11):3443

<sup>&</sup>lt;sup>46</sup> Art 3(10) Regulation (EC) No 178/2002

<sup>&</sup>lt;sup>47</sup> Art 23(b) Regulation (EC) No 178/2002

<sup>&</sup>lt;sup>48</sup> Art 40(1) Regulation (EC) No 178/2002

<sup>&</sup>lt;sup>49</sup> Art 40(3) Regulation (EC) No 178/2002

	manufacturing	
A copy of the studies	Covering independent, peer-reviewed studies	
A comparative analysis	Labeling proposal if the food characteristic is significantly different from the conventional counterpart, taking into account the natural variation in the product	
Ethical or religious concerns	Labeling proposal if the food would raise any issue related to ethical or religious concerns	
Placing on the market	Specific conditions for use and handling	
Detection methods	Detection methods, sampling, methods for detection of the transformation event, and methods to detect the transformation event in the food*	
Samples	Food and control samples, the reference materials	
Post market monitoring*	A proposal for post-market monitoring for the human consumption	
Summary of the dossier	In a standardised form	

# \*where applicable

The requirements for the authorisation of feed are quite similar. They are further clarified in Art 17(3) Regulation (EC) No 1829/2003. Moving on, Art 27 (1) Regulation (EC) No 1829/2003 emphasizes that when an applicant submits the dossiers for products intended for use as both food and feed, this must be accomplished by a single application and EFSA accordingly will give one opinion. This provision was cited after an incident involving StarLink<sup>TM</sup> corn. This GM corn, which contains a pesticidal protein (Cry9C), was approved by the Environmental Protection Agency (EPA) as animal feed. Later it was detected in Taco shells and human food. Subsequently, the EC also consider that the same issue may arise in the EU. To avoid the same liability issue, all of the producers which are applying GM feed in the EU are required to submit the application for the authorisation for food as well.

In cases of GM plants involving stacks, plants that contain more than one gene inserted or modified, EFSA will conduct a risk assessment on the basis of "a weight-of-evidence approach," which allows the EFSA to evaluate all of the plausible combinations and concerns regarding gene stability and safety outcome.<sup>51</sup> In accordance with Article 3(6) Reg. (EU) 503/2013, an applicant that has submitted a risk assessment dossier is also required to submit information pertaining to the stability of the transformation events, the expression of the transformation events, and any potential synergistic or antagonistic effects. The details of the risk assessment procedure in each step is defined thoroughly in the next section.

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<sup>&</sup>lt;sup>50</sup> Taylor, M. R., & Tick, J. S. (2001). *The StarLink Case: Issues for the Future*. Retrieved September 26, 2018 from <a href="http://www.rff.org/files/sharepoint/WorkImages/Download/RFF-RPT-StarLink.pdf">http://www.rff.org/files/sharepoint/WorkImages/Download/RFF-RPT-StarLink.pdf</a>

<sup>&</sup>lt;sup>51</sup> EFSA. (2011). Guidance on selection of comparators for the risk assessment of genetically modified plants and derived food and feed. *EFSA Journal*; 9(5):2149

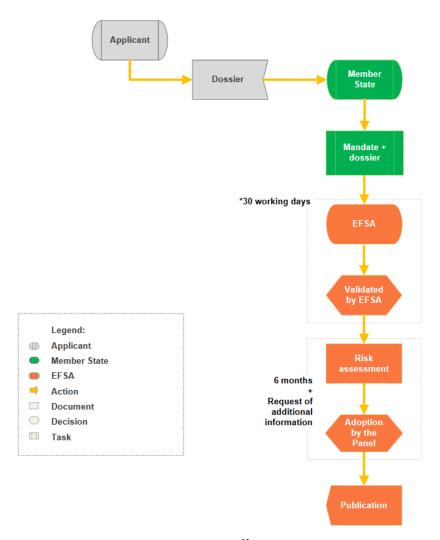


Figure 2.1 GMO application procedures<sup>52</sup>

The applicant dossiers received by the CA are transmitted to EFSA immediately and get validated within 30 working days. If EFSA finds any incomplete documents, they will request the applicant to revise them. If the results are satisfactory, the dossier will begin the risk assessment procedure, which will take approximately six months or longer. If there is any additional information needed before the material can be adopted by the Panel,<sup>53</sup> EFSA may ask the CA to conduct an e.r.a for GMOs intended for deliberate release to the environment.<sup>54</sup> The scientific opinion written by EFSA will be published in EFSA's journal, and the public may comment until 30 days after the publication of the journal.<sup>55</sup> This opinion will also be sent to the EC, the MS, and the applicant.<sup>56</sup>

 $<sup>^{52}\,</sup>EFSA.\,(2017).\,Application\,help desk-GMO\,application\,procedure.\,Retrieved\,September\,21,\,2018\,from\,\underline{https://www.efsa.europa.eu/sites/default/files/applications/apdeskapplworkflowgmo.pdf}$ 

<sup>&</sup>lt;sup>53</sup> Art 6(1) Regulation (EC)No 1829/2003

<sup>&</sup>lt;sup>54</sup> Art 6(3C) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>55</sup> Art 6(7) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>56</sup> Art 6(6) Regulation (EC) No 1829/2003

If applicable, the applicant may also request confidentiality for all application documents for the purpose of protection from competitors under Art 30(1) Regulation (EC)No 1829/2003. Under this section on data protection, it is stated that after ten years, all of the information in the dossiers can be openly accessed if the applicant can testify that their products are alike.<sup>57</sup>

This thesis will focus on describing the principle of risk assessment in order to provide answers regarding which kind of dossiers need to be submitted. The four principles which will be explained shortly are: molecular characterisation of the GM plant; comparative analysis of compositional, phenotypic and agronomic properties; safety assessment for humans and animals; and safety assessment for the environment.

#### 2.2.3.1 MOLECULAR CHARACTERISATION OF THE GM PLANT

This section provides information pertaining to the structure and manifestation of embedded genes. It will also address the steadiness of the designed plants' character, taking into account both safety concerns and the possibility that allergens or toxins that may emerge.

Table 2.2.3.1 Information required for the assessment of molecular characterisation according to Part II 1.2 Annex II to Regulation (EU) No 503/2013



Information about the genetic modification:

"Description of the methods"

"Nature and source of vector used"

"Source of donor nucleic acid(s) used for transformation, size and intended function of each constituent fragment of the region intended for insertion"



Information relating to the GM plant:

"General description of the trait(s) and characteristics"

"Information on the sequences"

"Information on the expression of the insert(s)"

"Genetic stability of the insert and phenotypic stability of the GM plant" "Potential risk associated

"Potential risk associated with horizontal gene transfer"



Supplemental information relating to the GM plant required for the environmental safety aspects:

"Information on how the GM plant differs from the recipient plant in reproduction, dissemination, survivability or other

"Any change to the ability of the GM plant to transfer genetic material to other organisms,

(a) Plant to bacteria gene transfer:

(b) Plant to plant gene transfer."

<sup>&</sup>lt;sup>57</sup> Art 31 Regulation (EC) No 1829/2003

# 2.2.3.2 COMPARATIVE ANALYSIS OF COMPOSITIONAL, PHENOTYPIC AND AGRONOMIC PROPERTIES

The comparative analysis step has the purpose of identifying the commonalities and variations between the GM plants/food/feed and the conventional analogue. For conducting these studies, several sets of data are needed, as stated in Part II 1.3 Annex II of Regulation (EU) No 503/2013 are required:



Figure 2.2.3.2 Steps of Comparative Analysis Procedure

The series above can be carried out only if the conventional analogue exists. In cases in which the GM crops are not closely related to any conventional plant, the safety and nutritional assessment shall be conducted under the novel food regulation scheme. <sup>58</sup> The method of choosing the additional comparators is regulated by the same section of Annex II of Regulation (EU) No 503/2013, which depends on the type of plant reproduction (vegetative/sexual), the characteristic of being either herbicide tolerant or not, and the potential for stacked transformation. The more detailed requirements are explained in the EFSA's guidelines. <sup>59</sup> The data from field trials, including the statistical analysis, are also needed at this step. Those can be found in different EFSA opinions. <sup>60</sup> In sum, the comparative analysis results should include information about whether the GM crops/food/feed is different from the conventional counterpart in terms of compositional, phenotipic, and agronomic properties, and whether a stack event with the conventional breeding leads to combinational events. <sup>61</sup>

#### 2.2.3.3 SAFETY ASSESSMENT FOR HUMANS AND ANIMALS

# 1. Toxicological assessment

The assessment of toxicological effects is intended to analyse the effects of the altered gene on the health of humans and animals. This assessment is established by Art 4(1-3) Regulation (EU) No 503/2013. These articles state that the toxicological studies shall not only rely on Directive 2004/10/EC, but also on 'OECD Principles on Good Laboratory Practice.' This directive also applies to assessments which are conducted outside the EU. Other relevant studies beyond toxicological

<sup>&</sup>lt;sup>58</sup> Part II 1.3 Annex II of Regulation (EU) No 503/2013

<sup>&</sup>lt;sup>59</sup> EFSA. (2011). Guidance on selection of comparators for the risk assessment of genetically modified plants and derived food and feed. *EFSA Journal*; 9(5):2149

<sup>&</sup>lt;sup>60</sup> EFSA. 2010. Statistical considerations for the safety evaluation of GMOs. EFSA Journal; 8(1):1250

<sup>&</sup>lt;sup>61</sup> Part II 1.3.7 Annex II of Regulation (EU) No 503/2013

studies should also be done in conformity with ISO standards. The applicant should also submit reviews of any other studies that have been issued in scientific journals or as self studies for the ten years prior to the appplication.<sup>62</sup>

Furthermore, in accordance with Part II 1.4 Annex I to Regulation (EU) No 503/2013, the applicant shall also submit the following information when applicable:



Figure 2.2.3 Components of GM plants toxicological assessment

The protocols and testing methods are further set forth in Tables 1 and 2 of Section 1.7 Annex II of Regulation (EU) No 503/2013, which also make reference to the testing methods stipulated in Annex of Regulation (EC) No 440/2008. For example, if a particular GM crop contains a newly expressed protein, a repeated-dose 28-day oral toxicity study in rodents must be conducted. The method for such a study is given in the table at B.7. The details of these protocols, including the test principles, procedures, data, and reporting, can be found in the Annex of Regulation (EC) No 440/2008.

The purposes of these toxicological assessments are described in the Implementing Regulation (EU) No. 503/2013. They include such things as evaluating the effects of GM plants (both unintended and intended), establishing the maximum dose and the acceptable daily intake (ADI), and describing any likelihood of adverse effects or uncertainties through the conducting of "90-day feeding studies." For reasons based on the properties of the GM plant or information contained in the research results, EFSA may ask the company to conduct supplemental studies. A common example would be the 90-day rodent feeding studies as part of the toxicological assessment. Additional guidance has been given by EFSA to augment "the OECD Guideline for the Testing of Chemicals – Repeated Dose 90-day Oral Toxicity Study in Rodents (OECD TG 408)." This study has generated diverse opinions among scientist and politician in the EU, and therefore in accordance with Article 12 Reg.No. 503/2013, "The Commission shall review the requirement to perform 90-day feeding studies in rodents . . . on the basis of new scientific information." This provision will be researched further by the seventh Framework Programme for Research (FP7), along with GRACE<sup>64</sup> and G-TwYST, <sup>65</sup> and

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 $<sup>^{62}</sup>$  Art 6(1) Regulation (EU) No 503/2013

<sup>&</sup>lt;sup>63</sup> EFSA. (2011). Guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. *EFSA Journal*;9(12):2438

<sup>&</sup>lt;sup>64</sup> GMO Risk Assessment and Communication Evidence. See more at <a href="http://www.grace-fp7.eu/en/content/project">http://www.grace-fp7.eu/en/content/project</a>

other projects funded by the Member States, e.g GMO90+ (French).<sup>66</sup> All of these projects exchange updates on their research outcomes in a manner that is transparent and open to the public.<sup>67</sup>

There are several reasons which have caused the authorities to become dubious regarding the implementation of 90-day feeding trials.<sup>68</sup> First, there has never been a consensus among scientists and various stakeholders as to whether the trial requirement is essential to the evaluation of GM food/feed safety.<sup>69</sup> Second, this additional study is inconsistent with international frameworks, such as the Codex guideline, which establish that substantial equivalence (par.13), compositional analysis (par.18), phenotypic information (par.24), and effect on human health through status as either toxin or antinutrient (par.26), are already sufficient. 70 Therefore, the studies may interfere with international trade, especially for other countries who do not impose any animal feeding study requirements during the process of risk assessment.<sup>71</sup> Furthermore, this method could not be used as a full assurance for food safety testing, because of some built-in limitations, such as the difficulties of extrapolation from animal to human, 72 and the ability to determine a proper sample size. 73 Third, an ethical issue has been raised about the necessity of this study.<sup>74</sup> FAO/WHO has stipulated that animal feeding trials are only needed when the existing data is insufficient to perform a meticulous risk assessment.<sup>75</sup> The EU regulatory framework through Directive 2010/63/EU on the protection of animals used for scientific purposes has set up the rule to "replace, reduce and refine the use of animals in procedures," 76 and rodents are included in the scope of this directive.<sup>77</sup> Lastly, the EU funded projects that are focusing on investigating the necessity of conducting these studies have not yet provide the answer. The study

<sup>&</sup>lt;sup>65</sup> Genetically modified plants Two Year Safety Testing. See more at <a href="https://www.g-twyst.eu/">https://www.g-twyst.eu/</a>

<sup>&</sup>lt;sup>66</sup> GMO90plus. See more at http://recherche-riskogm.fr/en/page/gmo90plus

<sup>&</sup>lt;sup>67</sup> Schiemann, J., Steinberg, P., & Salles, B. (2014). Facilitating a transparent and tailored scientific discussion about the added value of animal feeding trials as well as in vitro and in silico approaches with whole food/feed for the risk assessment of genetically modified plants. *Archives of toxicology*, 88(12), 2067-2069.

<sup>&</sup>lt;sup>68</sup> Devos, Y., Naegeli, H., Perry, J. N., & Waigmann, E. (2016). 90-day rodent feeding studies on whole GM food/feed: Is the mandatory EU requirement for 90-day rodent feeding studies on whole GM food/feed fit for purpose and consistent with animal welfare ethics? *EMBO reports*, e201642739.)

<sup>&</sup>lt;sup>69</sup> GRACE. (2015). Final results and recommendations of the EU research project GRACE. Retrieved November 3, 2018 from <a href="http://www.grace-fp7.eu/en/content/final-results-and-recommendations-eu-research-project-grace">http://www.grace-fp7.eu/en/content/final-results-and-recommendations-eu-research-project-grace</a>

<sup>&</sup>lt;sup>70</sup> Codex "Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants" (2003)

<sup>&</sup>lt;sup>71</sup> Ibid., 69

 $<sup>^{72}</sup>$  FAO. (2009). GM food safety assessment tools for trainer. Retrieved November 3, 2018 from <a href="http://www.fao.org/3/a-i0110e.pdf">http://www.fao.org/3/a-i0110e.pdf</a>

<sup>&</sup>lt;sup>73</sup> EFSA. (2014). Explanatory statement for the applicability of the Guidance of the EFSA Scientific Committee on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed for GMO risk assessment. *EFSA Journal*;12(10):3871

<sup>&</sup>lt;sup>74</sup> Ibid., 69

<sup>&</sup>lt;sup>75</sup> The Joint FAO/WHO Expert Consultation on Foods Derived from Biotechnology. (2000). *Safety aspects of genetically modified foods of plant origin*. Section 4.2, paragraph 4.2.2

<sup>&</sup>lt;sup>76</sup> Art 1(a) Directive 2010/63/EU

<sup>&</sup>lt;sup>77</sup> Art 3(a) Directive 2010/63/EU

performed by GRACE in 2014 revealed that the consumption of MON810 maize by rats at Wistar Han RCC did not indicate any detrimental effects. In April 2018, a study conducted by G-TwYS using GM maize NK603 also came to the conclusion that "no potential risk for humans and animals was identified" during the study. Considering the recent outcomes of the scientific research to date, there is a lack of evidence to justify the usefulness of mandatory 90-day feeding trials. It should be noted that the approach of the study conducted by EFSA is rather exploratory, rather than driven by hypothesis, since it takes into account the innate properties of GM plants that have never been identified as a risk.

# 2. Allergenicity

An allergen is different from a toxin. Allergens involve the immune systems of individual human bodies, and negative reactions are usually caused by the properties of proteins that are present in food. The reactions may be different in every person, depending on the genetic and atopic conditions found in individual bodies.<sup>81</sup> The allergenicity test is used to determine whether the GM crops tend to be similarly allergenic or more allergenic than the conventional analogue.<sup>82</sup> Part II 1.5 Annex II of Regulation (EU) No 503/2013 provides the lists of information resulting from allergenicity studies that must be submitted. These cover the assessment of newly expressed proteins and GM crops as a whole. By using 'a weight-of-evidence approach', the producers shall also following these kinds of procedures:<sup>83</sup>

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<sup>&</sup>lt;sup>78</sup> Zeljenková, D., Ambrušová, K., Bartušová, M., Kebis, A., Kovrižnych, J., Krivošíková, Z., ... & Szabová, E. (2014). Ninety-day oral toxicity studies on two genetically modified maize MON810 varieties in Wistar Han RCC rats (EU 7th Framework Programme project GRACE). *Archives of toxicology*, 88(12), 2289-2314.)

<sup>&</sup>lt;sup>79</sup> G-TwYS. (2018). *Conclusions and Recommendations*. Retrieved November 3, 2018 from <a href="https://www.g-twyst.eu/files/Conclusions-Recommendations/G-TwYSTConclusionsandrecommendations-final.pdf">https://www.g-twyst.eu/files/Conclusions-Recommendations/G-TwYSTConclusionsandrecommendations-final.pdf</a>

<sup>&</sup>lt;sup>80</sup> Hong, B., Du, Y., Mukerji, P., Roper, J. M., & Appenzeller, L. M. (2017). Safety assessment of food and feed from GM crops in Europe: Evaluating EFSA's alternative framework for the rat 90-day feeding study. *Journal of agricultural and food chemistry*, 65(27), 5545-5560.

<sup>81</sup> Part II 1.5 Annex II of Regulation (EU) No 503/2013

<sup>82</sup> Part II 1.5.4 Annex II of Regulation (EU) No 503/2013

<sup>83</sup> Part II 1.5.1 Annex II of Regulation (EU) No 503/2013

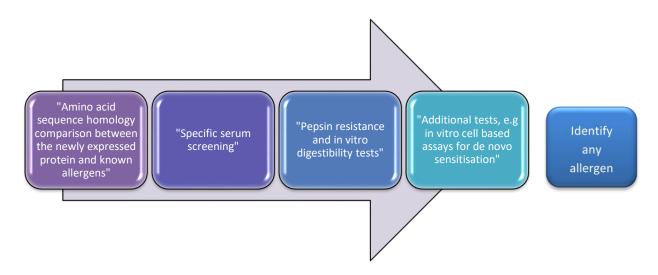


Figure 2.2.3 The process of allergenicity assessment

Further information on the application and requirements are written in EFSA's scientific opinion on the assessment of the allergenicity of GM plants and microorganisms and food and feed that is derived from them.<sup>84</sup>

# 3. Nutritional assessment

A nutritional assessment is carried out for GM crops intended for either food or feed. This test is designed to assess whether the GM products are nutritionally less beneficial to humans' vis-à-vis animals' health compared to the conventional counterpart. Furthermore, the inadvertent effects are also assessed to differentiate the influence of the nutritional component form the conventional counterpart. The things assessed include the nutrient and the anti-nutrient effects, bioavailability, and the anticipated human or animal intake. More information about how to conduct these studies is provided in the EFSA's journal. 88

#### 2.2.3.4 SAFETY ASSESSMENT FOR THE ENVIRONMENT

When producers are applying for GM crop cultivation, the MS, in accordance with Art 4(1) Directive 2001/18/EC, must ensure that these plants do not cause any harm to human health or the environment. Thus, the MS will ask the applicants conduct an e.r.a.<sup>89</sup> The e.r.a, according to Art 2(8), must address "the evaluation of risks to human health and the environment, whether direct or indirect, immediate or delayed, which the deliberate release or the placement on the market may impose and be carried out in

<sup>87</sup> Part II 1.6.2 Annex II of Regulation (EU) No 503/2013

<sup>&</sup>lt;sup>84</sup> EFSA. (2010). Scientific Opinion on the assessment of allergenicity of GM plants and microorganisms and derived food and feed. *EFSA Journal*; 8(7):1700

<sup>85</sup> Part II 1.6.1 Annex II of Regulation (EU) No 503/2013

<sup>86</sup> Ibid., 61.

<sup>&</sup>lt;sup>88</sup> EFSA. (2008). Safety and Nutritional Assessment of GM Plants and derived food and feed: The role of animal feeding trials. *Food and Chemical Toxicology* 46; S2–S70

<sup>89</sup> Art 4(2) Directive 2001/18/EC

accordance with Annex II". In March 2018, the EC has announced a new Commission Directive (EU) 2018/350 of 8 March 2018 amending Directive 2001/18/EC of the European Parliament and of the Council as regards the environmental risk assessment of GMOs. Pursuant to Article 1 of this Directive, the Annexes II, III, III B and IV to Directive 2001/18/EC are amended in line with the Annex to Directive 2018/350. The information required for the safety assessment of GM crops cultivation includes the following:<sup>90</sup>

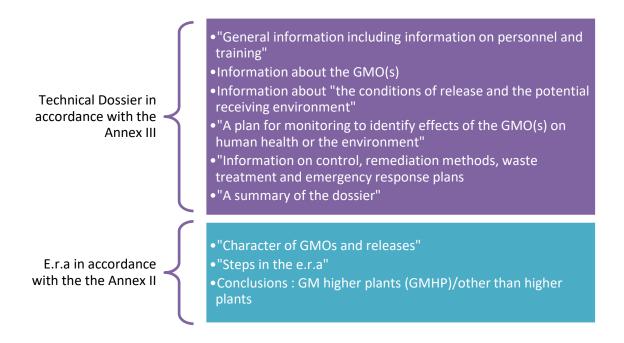


Figure 2.2.3.4 The information required for the e.r.a

Under Art 6(2) Directive 2001/18/EC, the applicant may also refer to a dossier which has been submitted by another applicant provided that these data are not confidential and the parties have signed an agreement.

The Annex IIb to Directive 2001/18/EC specifies general principles of the e.r.a as follows: (1) the e.r.a shall identify the "potential cause effects" of GMOs compared to the traditional products, (2) depend upon scientific principle and transparent way, (3) make use of "a case by case basis", and (4) provide an update whenever there is a new information available. Besides those principles that have been mentioned above, there are "general and specific considerations" that also must be taken into account, including, inter alia, changes which are intended and unintended, disadvantageous effects that could be long-term and cumulative long-term, quality of data, and events of stack transformation.<sup>91</sup>

Moving to the steps for conducting an e.r.a on GM crops, there are six phases required for this process as stated in Part C3 Annex II to Directive 2018/350. After following those steps, a conclusion

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<sup>90</sup> Art 6(2) Directive 2001/18/EC

<sup>91</sup> Part C1 Annex II of Directive 2001/18/EC

regarding its impact to the environment will be determined by assessing each aspect outlined in part D2 Annex II of the directive.

# 2.2.4 THE GM LABELING REGULATION IN THE EU

The labelling of GMOs is controlled by Regulation (EC) No 1829/2003. This regulation affects products intended for final consumers and mass caterers, 92 such as cafes, restaurants, or food stalls. However, Art 12(2) Regulation (EC) No 1829/2003 stipulates the exemption from mandatory labelling of products where the GM ingredients are maximum 0.9% of the total, in condition that this is either 'adventitious or technically unavoidable.'93 The food business operators (FBOs) have the burden of proving that they took reasonable steps to prevent this contamination. 94 The coexistence policy developed by the EC was an effort to sustain the segregation of GMOs from traditional products by developing national strategies and technical measures. 95 In addition, EFSA has published a guideline to determine a risk assessment for low levels of GMOs in food and feed. 96 A spatial isolation with various distances, for instance, has been taken as a precaution in the Netherlands and Luxemburg, which have created a buffer zone to prevent any cross pollination. 97

When GM foods fall under the scope of mandatory labelling, producers must include the words 'genetically modified' or 'produced from genetically modified (name of the ingredient)' in the written list of ingredients. <sup>98</sup> If the products are sold without any list, these words must be shown on the packaging. <sup>99</sup> The words 'not for cultivation' shall be put on the packaging and in the product records with the exception of products listed in point (a) of Article 2 of Regulation (EC) No 1830/2003. In situations where the products are sold without any packaging or it is not possible to put any written label on them, the GM information shall appear on the shelves or another place close to the products. <sup>100</sup> Additional information shall also be included if the products can be distinguished from non GM products, in particular the differences in: "i) composition; (ii) nutritional value or nutritional

<sup>92</sup> Art 12(1) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>93</sup> Art 12(2) Regulation (EC) No 1829/2003

<sup>94</sup> Art 12(3) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>95</sup> European Commission. (2012). Coexistence of genetically modified crops with conventional and organic agriculture.
Retrieved October 14, 2018 from <a href="https://ec.europa.eu/agriculture/gmo/coexistence\_en">https://ec.europa.eu/agriculture/gmo/coexistence\_en</a>

<sup>&</sup>lt;sup>96</sup> EFSA. Guidance for the risk assessment of the presence at low level of genetically modified plant material in imported food and feed under Regulation (EC) No 1829/2003. *EFSA Journal* 2017;15(11):5048

<sup>&</sup>lt;sup>97</sup> Dillen, K., Rizov, I., Cerezo, E. (2016). Developing Solutions for Coexistence in the EU—Legal, Technical, and Economic Issues, p.65. In: *The coexistence of genetically modified, organic and conventional foods: Government policies and market practices.* Kalaitzandonakes, N., Philips, P., Wesseler, J., Smyth, S (ed). Natural resource management and policy, volume 49. New York: Springer. doi:10.1007/978-1-4939-3727-1

<sup>&</sup>lt;sup>98</sup> Art 13(1a) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>99</sup> Art 13(1c) Regulation (EC) No 1829/2003

<sup>100</sup> Art 13(1e) Regulation (EC) No 1829/2003

effects; (iii) intended use of the food; (iv) implications for the health of certain sections of the population;"<sup>101</sup> and also "where a food may give rise to ethical or religious concerns."<sup>102</sup>

Besides the labelling, the producers are also obliged to include unique identifiers as stated in Art 4(1b) Regulation (EC) No 1830/2003. These systems shall be developed and evaluated by the EC prior to the implementation of traceability and labelling.<sup>103</sup>

# 2.2.5 CONCLUSION

The GM crops regulatory framework in the EU is governed by multi-governance, with the EFSA in the role of risk assessor, the EC as a risk manager, and both acting together to endorse a risk communication process. The EU regulations, together with the precautionary principle, have established that GMOs must follow this authorisation procedure prior to the distribution of GMOs to the market or deliberate release to the environment. The risk assessment procedure is an essential component of this procedure, as is highlighted in this context. There are four steps that must be followed: molecular characterisation of the GM plant; comparative analysis of compositional, phenotypic and agronomic properties; safety assessment for humans and animals; and safety assessment for the environment.

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<sup>&</sup>lt;sup>101</sup> Art 13(2a) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>102</sup> Art 13(2b) Regulation (EC) No 1829/2003

<sup>&</sup>lt;sup>103</sup> Art 8(1a) Regulation (EC) No 1830/2003

# 2.3 THE AMERICAN LEGAL SYSTEM WITH REGARD TO THE GM CROPS REGULATION

# 2.3.1 THE REGULATORY FRAMEWORK OF THE GM CROPS IN THE US

Genetically engineered products and conventional products are regulated by the same statutory framework in the US, based on the assumption that both types carry the same risk in terms of health, safety, and impact on the environment. The GE products are therefore governed by a complex network of regulations that are promulgated by a variety of Federal agencies.<sup>104</sup>

In effect, GM foods in the US are treated the same as traditional food sources by the Food and Drug Administration (FDA) under Federal Food, Drug, and Cosmetic (FD&C) Act, with the exception of meat, poultry and egg products, which are regulated by the Food Safety Inspection Service (FSIS). In most cases, foods derived from engineered crops will fall into the category of GRAS, since the final products cannot be distinguished from their conventional counterparts. However, if the GM foods cannot be categorised as GRAS in compliance with 21 U.S. Code § 348, due to their having a different compound or an inadvertent effect, the products are then required to follow an authorisation procedure prior to their distribution to the market. To determine which category would apply, every new plant variety that contains a novel protein shall be submitted to a safety evaluation. This establishment of "early food safety evaluation" as a requirement is in accordance with the Coordinated Framework for the Regulation of Biotechnology Products, 106 which was updated in 2017. To guide the industry in complying with the applicable regulatory framework, the FDA has created guidelines. 107 Since its status is not binding, producers have the freedom to develop alternative approaches, as long they conform to the biotechnology regulatory framework. In such cases, it is highly recommended that the producers refer to the guidelines from CODEX. 108

GM crops which may pose a plant pest risk and are intended to be field tested prior to interstate movement and cultivation fall into the statutory framework coordinated by the United States Department of Agriculture; the Animal and Plant Health Protection Service (USDA-APHIS); the Plant Protection Act (PPA); and APHIS regulation. In cases where a GM plant pose any risk as a plant pest

<sup>&</sup>lt;sup>104</sup> Fish, A., Foxkiser., Rudenko, L. 2014. Guide to U.S. Regulation of Genetically Modified Food and Agricultural Biotechnology Products. Retrieved October 11, 2018 from <a href="https://www.pewtrusts.org/~/media/legacy/uploadedfiles/www.pewtrustsorg/reports/food">https://www.pewtrusts.org/~/media/legacy/uploadedfiles/www.pewtrustsorg/reports/food</a> and biotechnology/hhsbiotech0901

<sup>&</sup>lt;sup>105</sup> FSIS. 2015. Memorandum of Understanding between the Food Safety and Inspection Service United States Department of Agriculture and the Food and Drug Administration United States Department of Health and Human Services. Retrieved October 12, 2018 from <a href="https://www.fsis.usda.gov/wps/portal/fsis/topics/regulations/directives/7000-series/mou-fsis-fda">https://www.fsis.usda.gov/wps/portal/fsis/topics/regulations/directives/7000-series/mou-fsis-fda</a>

<sup>&</sup>lt;sup>107</sup> FDA. (2006) Guidance for Industry: Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use. Retrieved October 5, 2018 from <a href="https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Biotechnology/ucm096156.htm">https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Biotechnology/ucm096156.htm</a> #ftn6

<sup>&</sup>lt;sup>108</sup> FAO. (2003) Guideline for the Conduct of Food Safety Assessment of Foods Derived From Recombinant-DNA Plants. Retrieved October 5, 2018 from http://www.fao.org/fileadmin/user\_upload/gmfp/docs/CAC.GL\_45\_2003.pdf

as listed in 7 USC § 7702(14), its movement and importation are forbidden without specific authorisation. If necessary, the USDA may hold the distribution of the product or even destroy it to control the spreading of plant pest.<sup>109</sup>

Plant pesticides containing plant-incorporated protectants are regulated by the EPA under FIFRA, and the tolerance is set by the FD&C Act. The registration process for plant pesticides under FIFRA is a unique one, since this process includes a risk-benefit calculation that is usually not a factor in any other statutes. After following the registration process as described in Table 2.3.1, the pesticide must also comply with the labelling requirement, pursuant to 7 U.S. Code § 136(q). Selling any pesticide that is unregistered, misbranded, or adulterated in the US is considered an unlawful act. When any of these violations is found, the EPA has the right to remove the pesticide from the market and penalize the producers. To overcome the challenges to the development of GMOs, particularly for GM crops, each agency has divided the roles and tasks as follows:

Table 2.3.1 Oversight of GM plants and linked coordination between EPA, FDA, and USDA after the update in 2017<sup>113</sup>

Product Area	GM plants
Food for humans	-USDA/APHIS If plant poses a plant pest risk -FDA/CFSAN <sup>114</sup> -EPA/OPP <sup>115</sup>
Food for animals	- <u>USDA/APHIS</u> If plant poses a plant pest risk -FDA/CVM -EPA/OPP
Pesticide	-EPA/OPP -USDA/APHIS If plant poses a plant pest risk -FDA/CFSAN -FDA/CVM

Source: EPA, 2017

<sup>&</sup>lt;sup>109</sup> 7 U.S. Code § 7714

<sup>&</sup>lt;sup>110</sup> Wozniak, C., McClung, G., A., Gagliardi., J., Segal, M., Mattthews, K. (2012) Regulation of Genetically Engineered Microorganisms Under FIFRA, FFDCA and TSCA, p.71. In *Regulation of agricultural biotechnology: The United States and Canada*. Wozniak, C., & McHughen (Ed.) Dordrecht: Springer. doi:10.1007/978-94-007-2156-2

<sup>&</sup>lt;sup>111</sup> 7 U.S. Code § 136j(a-b)

<sup>&</sup>lt;sup>112</sup> 7 U.S. Code § 136k(a-b)

<sup>&</sup>lt;sup>113</sup> EPA. 2017. *Modernizing the Regulatory System for Biotechnology Products: Final Version of the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology*. Retrieved September, 29 2018 from <a href="https://www.epa.gov/sites/production/files/2017-01/documents/2017\_coordinated\_framework\_update.pdf">https://www.epa.gov/sites/production/files/2017-01/documents/2017\_coordinated\_framework\_update.pdf</a>

<sup>&</sup>lt;sup>114</sup> Center for Food Safety and Applied Nutrition (FDA)

<sup>&</sup>lt;sup>115</sup> Office of Pesticide Programs (EPA)

# 2.3.2 THE REGULATIVE POWER AND THE ROLE OF NON FEDERAL AGENCIES

GM crops in the US are subject to regulatory oversight by the Coordinated Federal Framework for the Regulation of Biotechnology, which is based on the existing legislation and governed by the FDA, EPA, and USDA-APHIS. This framework is based on an assessment of the final product, accomplished on a case-by-case review, and an exemption is given to GM products which do not differ significantly from their conventional counterparts. <sup>116</sup> In March 2018, the USDA secretary announced that new breeding techniques are also discharged, except those which apply to plant pest. <sup>117</sup> A modernisation of the Regulatory System for Biotechnology Products had been drafted by the Biotechnology Working Group (Biotechnology WG) in the previous year. This process brought several changes, especially in the roles of the regulatory agencies, which had not been updated in the previous sixteen years. This update provided better insight and enhanced public confidence with the goal of eliminating any superfluous hurdles in the GMOs regulatory regimes. <sup>118</sup> Some regulatory barriers still exist, such as the considerable costs and the unpredictability of the outcomes. This creates unfavourable conditions for small companies. <sup>119</sup>

# 2.3.2.1 FOOD AND DRUG ADMINISTRATION

The FDA has the responsibility for monitoring and ensuring food safety for humans and animals, including the safety of GM products, which to date have the same stringency as non GM foods. <sup>120</sup> Also included are some natural products, such as sweet potatoes, which may inherently contain small amounts of foreign genes (such as soil bacteria). <sup>121</sup> Gene editing techniques, including recombinant DNA, are continuations of conventional breeding according the FDA. They share the common goal of improving the quality of plants, and therefore are judged only in the final products, rather than in their processes. <sup>122</sup> The regulatory oversight encompassing GM crops seeks improvements in nutritional contents, resistance to chemical herbicide, and improvements to flavour or texture. <sup>123</sup>

The modified crops intended for foods are part of the FDA's oversight. They may be categorised either as Generally Recognized as Safe (GRAS) or belong to the category of food additives. The definition of food is found in 21 USC § 321(f), which states in part that food includes, "(1) articles

<sup>&</sup>lt;sup>116</sup>Wozniak, C., Waggoner, A., Reilly, S. 2012. An Introduction to Agricultural Biotechnology Regulation in the U.S, p.5. In *Regulation of agricultural biotechnology: The United States and Canada*. Wozniak, C., & McHughen (Ed.) Dordrecht: Springer. doi:10.1007/978-94-007-2156-2

<sup>117</sup> Ibid., 23

<sup>118</sup> Ibid., 113

<sup>119</sup> Ibid., 14

<sup>&</sup>lt;sup>120</sup> FDA. 2018. How FDA Regulates Food from Genetically Engineered Plants. Retrieved October 2, 2018 from <a href="https://www.fda.gov/Food/IngredientsPackagingLabeling/GEPlants/ucm461831.htm">https://www.fda.gov/Food/IngredientsPackagingLabeling/GEPlants/ucm461831.htm</a>

<sup>&</sup>lt;sup>121</sup> Vincelli, P. 2017. *Genetically Engineered Crops Emerging Opportunities*. Retrieved October 12, 2018 from <a href="http://www2.ca.uky.edu/agcomm/pubs/PPA/PPA47/PPA47.pdf">http://www2.ca.uky.edu/agcomm/pubs/PPA/PPA47/PPA47.pdf</a>

<sup>122</sup>Ibid

<sup>&</sup>lt;sup>123</sup> FDA. 1992. Statement of Policy - Foods Derived from New Plant Varieties. Retrieved October 5, 2018 from https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Biotechnology/ucm096095.htm

used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article." The term "food additive" is explained in 21 USC § 321(s) as, "any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food." GM crops can be included into the latter if there has not been an agreement among scientists that its components are unsafe, or that its effects are still debatable. Since GM products have been introduced in the US for more than thirty years without any harmful effect, most GMOs fall into the GRAS category. Producers must only participate in voluntary consultations, although in reality they often become compulsory. The FDA may also assert that certain products are GRAS and release that information to the public. Infrequently, GM foods are categorised as food additives if the final products are significantly different from the non-GM foods. Under 21 U.S. Code § 348, these products must be submitted to a premarket approval process before they may be distributed to the market. These requirements are detailed in the proposed rule, 66 FR 4706.

Besides these existing regulations, there are also guidelines that were developed by the US Secretary of Health and Human Services. Although not binding for them, the secretary may force the FDA to conform with these guidelines if there is not any justification to object <sup>126</sup> to this guidance on the agency's own motion. <sup>127</sup> This guideline is also not binding on the public, including business operators, as long as the producers could conclusively provide an alternative approach which would demonstrate their acquiescence to the statutes. <sup>128</sup> The producers are also encouraged to follow these consultations with the FDA while this guidance is being developed. <sup>129</sup> However, considering the complexity of creating a different approach, many applicants will choose to simply follow the agency's guidance. This would be prudent if, for instance, the guidance procedure concerned "safety evaluation for new non-pesticide proteins from new plant varieties". <sup>130</sup> Moreover, the agency may also refuse the application if the submitted report is incomplete or has an obscure result. <sup>131</sup>

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<sup>124</sup> Ibid., 14

<sup>125 21</sup> CFR §170.35

<sup>126 21</sup> U.S.C §371h-1(a)(b)

<sup>127 21</sup> C.F.R §10.115

<sup>128</sup> Ibid

<sup>129</sup> Ibid

<sup>&</sup>lt;sup>130</sup> FDA. 2006. Guidance for Industry: Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intesnded for Food Use. Retrieved October 2, 2018 from <a href="https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm096156.htm">https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm096156.htm</a>

<sup>131 21</sup> CFR 71.1(d)

After following the consultation procedure, producers must continue to monitor their products in the marketplace to insure compliance with the regulations. Any deviation from the statutes will lead to FDA warning letters, confiscation, product recalls, and even criminal indictments.<sup>132</sup>

# 2.3.2.2 THE USDA-ANIMAL AND PLANT HEALTH INSPECTION SERVICE

APHIS is one of the agencies in the USDA which is tasked with the regulation of GM crops before their introduction into the environment (including field testing), importation, or interstate movement. 133 This provision is further explained in the Biotechnology Regulations Services (BRS), which are in line with 7 C.F.R. §340. GM crops will be able to enter the marketing process only after the producers can prove that their products do not carry higher risks to agriculture compared with their conventional counterparts. 134 They must also follow the safety and environmental assessment procedures. After meeting those requirements, either through the notification or the permitting procedure, these products do not require further regulation and can be freely distributed in the US market. 135 Furthermore, APHIS also adheres to the National Environmental Policy Act (NEPA) as the foundation for protection of the environment, <sup>136</sup> which is outlined in 7 C.F.R. §372. In situations where there is a reason to believe that a particular GM plant is a plant pest as listed in 7 CFR §340.2a, an authorisation procedure is required. 137 Exemptions are given for limited interstate movement for plant pests which hold the genotypes Escherichia coli (strain K-12 and its derivatives), Saccharomyces cerevisiae, Bacillus subtilis, and Arabiodopsis thaliana. 138 It is also possible to create a petition to modify the list of plant pests by submitting the petition to APHIS, which may exempt GM crops as "regulated articles." <sup>139</sup> It is expected, however, that APHIS will be more prudent in the future in deciding which plants will be exempted from the regulation, because previously the deregulation of GE Monsanto alfalfa before the completion of an 'environmental impact statement' (EIS) caused massive protests from organic farmers who eventually won a lawsuit since APHIS had breached the NEPA's provisions. 140

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<sup>&</sup>lt;sup>132</sup> FDA. 2008. Compliance & Enforcement. Retrieved October 2, 2018 from https://www.fda.gov/Food/ComplianceEnforcement/default.htm

 $<sup>^{133}</sup>$  USDA. 2018.  $Biotechnology\ Regulation\ Services$ . Retrieved October 3, 2018 from <a href="https://www.aphis.usda.gov/biotechnology/downloads/BRS\_Strategic\_Plan.pdf">https://www.aphis.usda.gov/biotechnology/downloads/BRS\_Strategic\_Plan.pdf</a>

<sup>&</sup>lt;sup>134</sup> APHIS. 2016. *Permits, Notifications, and Petitions*. Retrieved October 3, 2018 from <a href="https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions/ct\_submissions\_home">https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions/ct\_submissions\_home</a>

<sup>&</sup>lt;sup>135</sup> USDA. n.d. *How the Federal Government Regulates Biotech Plants*. Retrieved October 3, 2018 from <a href="https://www.usda.gov/topics/biotechnology/how-federal-government-regulates-biotech-plants">https://www.usda.gov/topics/biotechnology/how-federal-government-regulates-biotech-plants</a>

<sup>136 40</sup> C.F.R. §1500.1

<sup>137 7</sup> C.F.R §340 of PPA

<sup>138 7</sup> CFR §340.2a

<sup>139 7</sup> C.F.R. §340.5

<sup>&</sup>lt;sup>140</sup> Geerston Seed Farms v. Johanns, 541 F.3d 938 (2008)

As such, in response to shifting legislation, in June 2018, APHIS announced a notice of intent (NOI) to establish an EIS that will contain an impact analysis of GMOs regarding agriculture and forestry, agronomic practices, and the physical and biological environments. Another important change is a plan to analyse the socioeconomic impact of GMOs in the agricultural field, both inside the US and international trade. As a plan to analyse the socioeconomic impact of GMOs in the agricultural field, both inside the US and international trade.

# 2.3.2.3 ENVIRONMENTAL PROTECTION AGENCY

The EPA holds responsibility for the regulation of pesticide residues in food. 143 Concerning GM plants, the EPA's task is to oversee plant pesticides that are produced from GE tools that may pose an impact to the environment or to the health of humans, animals, or plants. 144 The EPA may require the applicant to submit information concerning the product's chemistry, toxicology, environmental fate, and residue. 145 Examples of GM plants that have been regulated by the EPA include, inter alia, GM crops that are intended to fight insects, bacteria, or fungus, and which belong to the category of pesticides. 146 Plant pesticides normally will produce plant-incorporated protectants, 147 which have unique abilities and different characteristics when compared to their conventional counterparts in the combating of plant pests. These traits meet the definition of pesticide according to 7 USC § 136(u). Examples of plant pesticides that have been approved by the EPA are Bacillus thuringiensis (BT) Cry9C in corn, BT Cry1A(b) in all plants, and BT Cry3A in potatoes. 148 Those plants, together with the other plant-incorporated protectants such as (BT) Vip3Aa in cotton or corn, BT Cry1A.105 in soybean, etc., are exempted from the requirement of residue tolerance either in food, feed, or both. 149 If the scale of field testing includes more than 10 acres of land per pest, the producers are also required to apply for experimental use permits (EUP). 150 The GM plants subject to this testing that are intended to be used as food for human or animals, or used in the production of processed food, are subject to the

<sup>&</sup>lt;sup>141</sup> USDA. 2018. *Updating Biotechnology Regulations*. Retrieved October 3, 2018 from <a href="https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/2017">https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/2017</a> perdue proposed rule/340 2017 perdue biotechreg

<sup>&</sup>lt;sup>142</sup> APHIS. 2018. *Notice of Intent To Prepare an Environmental Impact Statement; Movement and Outdoor Use of Certain Genetically Engineered Organisms*. Retrieved October 3, 2018 from https://www.aphis.usda.gov/brs/fedregister/BRS\_20180629.pdf

<sup>143 21</sup> U.S.C §346a

<sup>&</sup>lt;sup>144</sup> Ibid., 113

<sup>145 40</sup> C.F.R. § 158

<sup>146</sup> Ibid., 123

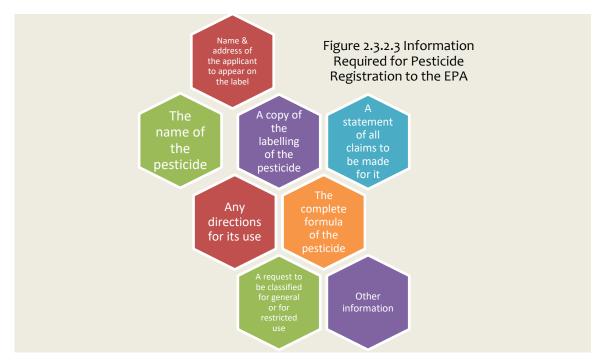
<sup>&</sup>lt;sup>147</sup> Plant-incorporated protectants are pesticidal substances produced by plants and the genetic material necessary for the plant to produce the substance. See more at <a href="https://www3.epa.gov/pesticides/chem\_search/reg\_actions/pip/index.htm">https://www3.epa.gov/pesticides/chem\_search/reg\_actions/pip/index.htm</a>

<sup>&</sup>lt;sup>148</sup> National Research Council (US) Committee on Genetically Modified Pest-Protected Plants. Genetically Modified Pest-Protected Plants: Science and Regulation. Washington (DC): National Academies Press (US); 2000. 1, Introduction and Background. Retrieved October, 1 2018 from https://www.ncbi.nlm.nih.gov/books/NBK208345/

<sup>&</sup>lt;sup>149</sup> 40 CFR Part 174, Subpart W

<sup>150 40</sup> C.F.R. § 172.3

provision of 21 U.S. Code § 346a, which controls the limits of pesticide residue. For pesticide registration, the producers are required to submit data as follows:<sup>151</sup>



Other information, such as test descriptions and results, may also be requested by the EPA in accordance with the next article. Afterward, the application will be reviewed, and revisions may be requested if needed. In addition, the EPA will also check to ensure that the submitted application is not similar to a registered pesticide or insufficiently different in composition. They will always take into account the dangers of "unreasonable adverse effects on the environment", which refers to, "(1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under section 346a of title 21." In accordance with the provision of 7 U.S. Code § 136a, the pesticide is not allowed to be sold without first having been registered in the EPA's database for the purpose of avoiding any "unreasonable adverse effects on the environment." This registration will be valid for fifteen years and will need to be reregistered after that. 155

<sup>&</sup>lt;sup>151</sup> 7 U.S. Code § 136a - Registration of pesticides

<sup>152</sup> Ibid

<sup>153</sup> Ibid

<sup>&</sup>lt;sup>154</sup> 7 USC § 136(bb)

<sup>155 7</sup> U.S.C. § 136a(g)

Table 2.3.2.3 Overview of EPA Regulation of Biotechnology Products: Plant-Incorporated Protectants

Legal Statues	FIFRA (EPA) Sec 2. Pesticide Definition Sec 3. Registration Sec 5. EUP	FD&C Act (FDA) Sec 408. Tolerance
Pre-market testing process	-Tolerance/tolerance exemption -EUP	
Pre-market testing regulatory process for distribution/use	-Tolerance/tolerance exemption -Registration	
EPA responses	-Issue/do not issue a registration -Issue/do not issue a tolerance exemp	tion

Source: EPA, 2017<sup>156</sup>

To summarise, the use of GMOs in the US is regulated by the three main agencies (the FDA, APHIS-USDA, and EPA). The national disclosure standard that was enacted in 2016 overrides any individual state's legislation concerning GMOs. This topic will be discussed further in the section on GM labelling in section 2.3.4 and state legislation in section 2.3.5.

# 2.3.3 SAFETY ASSESSMENT PROCEDURE OF GM CROPS

An "early food safety evaluation" by the FDA is the first step of the safety assessment for GM crops that contain a new protein and are intended for use as food. When the data submitted by an applicant indicates that their product might cause an allergic response or contain a toxic compound, a secondary assessment may need to be conducted. The decision tree of evaluation and additional test can be seen below (**Figure 2.3.3**).

<sup>156</sup> Ibid., 113

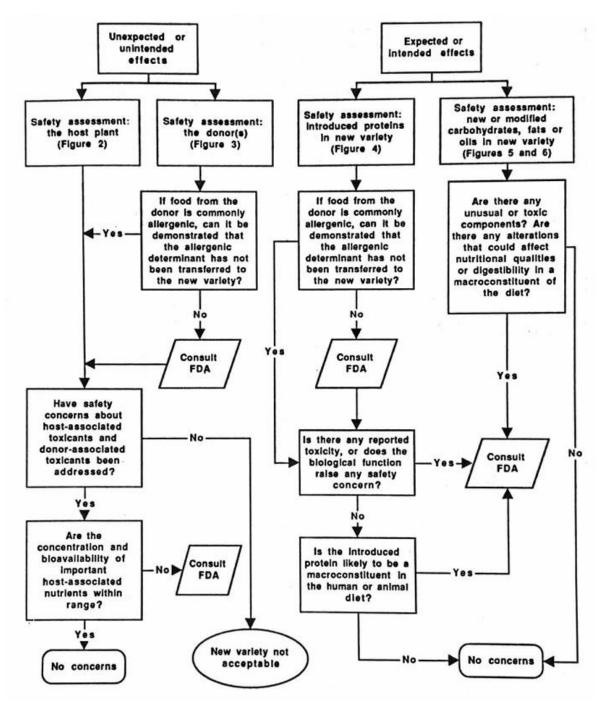


Figure 2.3.3 The safety assessment of new plant varieties

Source: FDA, 1992157

# 2.3.3.1 SUBSTANTIAL EQUIVALENCE

The substantial equivalence test is a process to be used in comparing GM plants with their conventional counterparts. This term was first mentioned in the Premarket Notification 510(k) for marketing a device. This principle was adopted by the FDA in their Statement of Policy for new plant

<sup>157</sup> Ibid., 123

varieties intended for foods in 1992. <sup>158</sup> This practical tool was adopted at a time when taking additional concerns into consideration was not yet thought to be important. The potential dangers from the consumption of biotechnology products were unforseen at the time. <sup>159</sup> In 1993, the OECD also released their report stating that that GMOs should receive the same treatment as traditional products, as long as they both offered the same level of risk. <sup>160</sup> In cases where there was a difference, the risk assessment was to focus on assessing the difference. <sup>161</sup>

In the application of this principle during the safety assessment, several aspects need to be considered as follows: the safety concerns associated with the introduction of the genetic material; the impacts on the metabolic pathways of humans or animals, which may have effects that are toxic to health; and the stability of the new trait that has been created. 162

### 2.3.3.2 ASSESSMENT OF TOXICITY AND NUTRIENT COMPOSITION

The nutrient component and bioavailability must be considered during the risk assessment, especially for animal feed. Over fifty percent of animal feed is produced from GM corn. <sup>163</sup> The nutrient change and toxicant do not profoundly influence human consumption, but this feed is consumed by animals in such significant amounts that this change could result in a lack of nutrient or a dietary shift in animals that may need to be complemented by other nutrients. <sup>164</sup> Under 21 U.S. Code § 342, a food which contains high toxicant level is referred to as an adulterated food and is prohibited from entering the market. In very rare cases, a conventional breeding technique may also result in a plant that is high in toxicants, such as the Lenape potato, which had to be withdrawn from the US market in 1977 because it contained high levels of glycoalkaloids. <sup>165</sup> To meet this provision, the responsibility of ensuring the safety of food products is held by the producers, and the FDA will oversee it through the regulatory process. Concerning GM foods, pursuant to the Coordinated Framework for Regulation of Biotechnology, some of them will be regulated as food additives, unless they fall into the scope of GRAS. <sup>166</sup> To be recognized as GRAS, a substance must meet safety requirements that are based on

<sup>158</sup> Ibid., 123

 $<sup>^{159}</sup>$  Schauzu,M. (2000). The concept of substantial equivalence in safety assessment of foods derived from genetically modified organism. AgBiotechNet., Vol.2 April, ABN 044

<sup>&</sup>lt;sup>160</sup> Organisation for Economic Co-operation and Development (Paris). (1993). Safety evaluation of foods derived by modern biotechnology: Concepts and principles (Engelse ed.). Paris: OECD.

<sup>161</sup> Ibid

<sup>162</sup> Ibid., 123

<sup>163</sup> Ibid

<sup>164</sup> Ibid

<sup>&</sup>lt;sup>165</sup> Osman, S. F., Zacharius, R. M., Kalan, E. B., Fitzpatrick, T. J., & Krulick, S. (1979). Stress metabolites of the potato and other solanaceous plants. *Journal of Food Protection*, 42(6), 502-507.

 $<sup>^{166}</sup>$  Ibid

scientific procedures, or had been used as common foods before January 1, 1958, both in the US and abroad. 167

#### 2.3.3.3 ASSESSMENT OF ALLERGENICITY

In most cases, good practices that were implemented by producers should eliminate unintended effects and toxins from GM crops. However, new substances including proteins and other nutrients may occur during the editing process, and this may result in significant differences from the conventional crop. <sup>168</sup> Thus, during the safety assessment for manipulated crops with new proteins, either the in vivo or in vitro test is required. A suitable testing requirement should be first be discussed with the FDA. If such an allergen is identified, the product is subject to a labeling requirement.

# 2.3.3.4 ASSESSMENT OF ENVIRONMENTAL IMPACT

When the GM crops are plant pest or there is a reason to believe that these products belong to plant pest, the APHIS has the authority to governing these GM crops under 7 CFR Part 340. The producers shall notify this agency 10 days before the introduction for movement between states, or 30 days if the introduction is for importation or designed to deliberate release into the environment. On the other side, APHIS will have ten days to respond for GM crops with regard to interstate movement, and thirty days for both importation and environmental release. This guideline is not mandatory as applied to the producers, and thus, they can develop their own approach. Consultation with APHIS may help, but it is not obligatory. Nonetheless, these main procedures should be followed for the notification procedure directed to the APHIS include the information listed in **Table 2.3.3**.

Furthermore, the report which contains the result of the field test which covered APHIS reference number, methods, resulting data, and impact analysis on plants and environments should be submitted in a period of six months after the experiment finished.<sup>172</sup> Nevertheless, the access to location and facilities of the experiments shall be granted to the APHIS to verify the data submitted.<sup>173</sup>

After notifying the APHIS, the next step is to apply for permit. Two copies of documents need to be submitted to APHIS under the condition that if any confidential business information (CBI) exist, the

<sup>167 21</sup> CFR 170.30

<sup>&</sup>lt;sup>168</sup> Ibid., 123

<sup>&</sup>lt;sup>169</sup> 7 CFR 340.3(d)(3)

<sup>170 7</sup> CFR 340.3(e)

<sup>171 7</sup> CFR 340.3

<sup>&</sup>lt;sup>172</sup> 7 CFR 340.3(d)(4)

<sup>173 7</sup> CFR 340.3(d)(6)

part of which CBI lay down need to be removed and marked with "CBI Deleted".<sup>174</sup> If none in the documents contains CBI, the first page of both documents required to state "No CBI".<sup>175</sup>

To apply for a permit designed for environmental release, producers need to hand in the report prior to 120 days before the release, and it is expected that the initial feedback will be sent by APHIS within 30 days. The Within 120 days from the application, a comprehensive review of APHIS will be finished and sent back to the applicant. However, the applicant may also be requested to deliver a supplementary information which cause the 120 days-review will restart at the day of additional information is received by APHIS, which delay the permit issuance. The data which shall be provided are described in **Table 2.3.3.4.** 

<sup>&</sup>lt;sup>174</sup> 7 CFR 340.4(a)

<sup>175</sup> Ibid

<sup>&</sup>lt;sup>176</sup> 7 CFR 340.4(b)

<sup>177</sup> Ibid

Table 2.3.3.4 List of Dossiers for APHIS submission

	Type of Event	
Type of the Document	Notification <sup>178</sup>	Permit <sup>179</sup>
Information of the responsible person	Name, title, address, telephone number, and signature	<ul> <li>Name, title, address, telephone number, signature</li> <li>"Type of permit requested (for importation, interstate movement, or release into the environment)"</li> </ul>
Information of the persons who developed and/or supplied the regulated article	-	- Names, addresses, and telephone numbers
Information about the regulated article(s)	"(A) The scientific, common, or trade names, and phenotype of regulated article,  (B) The designations for the genetic loci, the encoded proteins or functions, and donor organisms for all genes from which introduced genetic material was derived, and  (C) The method by which the recipient was transformed;"	<ul> <li>(A) "All scientific, common, and trade names, and all designations necessary to identify the: Donor organism(s); recipient organism(s); vector or vector agent(s); constituent of each regulated article which is a product; and, regulated article"</li> <li>(B) "A description of the means of movement (e.g., mail, common carrier, baggage, or handcarried (and by whom))"</li> <li>(C) "A description of the anticipated or actual expression of the altered genetic material in the regulated article and how that expression differs</li> </ul>
		from the expression in the non-modified parental organism"  (D) "A detailed description of the molecular biology of the system (e.g., donor-recipient-vector) which is or will be used to produce the regulated article;"  (E) "Country and locality where the donor organism, recipient organism, vector or vector agent, and regulated article were collected, developed, and produced;"

<sup>&</sup>lt;sup>178</sup> 7 CFR 340.3 (d)(1)(2)

<sup>&</sup>lt;sup>179</sup> 7 CFR § 340.4

		(F) "A detailed description of the purpose for the introduction of the regulated article including a detailed description of the proposed experimental and/or production design;"
		(G) "The quantity of the regulated article to be introduced and proposed schedule and number of introductions;"
Information of the movement or the environmental release	<ul> <li>The names and locations of the origination and destination facilities</li> <li>The size of the introduction</li> <li>The expected duration of the introduction (release)</li> </ul>	(A) "A detailed description of the processes, procedures, and safeguards which have been used or will be used in the country of origin and in the United States to prevent contamination, release, and dissemination in the production of the: Donor organism; recipient organism; vector or vector agent; constituent of each regulated article which is a product; and regulated article;"
		(B) "A detailed description of the intended destination (including final and all intermediate destinations), uses, and/or distribution of the regulated article (e.g., greenhouses, laboratory, or growth chamber location; field trial location; pilot project location; production, propagation, and manufacture location; proposed sale and distribution location);"
		(C) "A detailed description of the proposed procedures, processes, and safeguards which will be used to prevent escape and dissemination of the regulated article at each of the intended destinations;"
		(D) "A detailed description of any biological material (e.g., culture medium, or host material) accompanying the regulated article during movement; and"
		(E) "A detailed description of the proposed method of final disposition of the regulated article."
Additional requirement(s)	A statement that certifies that introduction of the regulated article in line with the regulation	-

The producers could also create a petition to modify the list of plant pests to the APHIS. 180 The following process should comply with NEPA provision which its importance could be seen from the case studies of "Roundup Ready alfalfa" (RRA) and "Roundup Ready sugar beets (RRSB). 181 In 2005, APHIS has set out the unregulated status of RRA under 70 FR 36917-36919 which attracted more than 600 public comments. 182 APHIS has also announced that the chance of RRA will pose any environmental risk to conventional alfalfa was at most improbable, since the buffer zone to avoid any cross pollination has been enacted. 183 However, this unregulated status was overturned by the US District Court for the Northern District of California following the lawsuit from Geertson together with other organic farmers, who demanded that GM alfalfa needs to be regulated since it may cause genetic contamination to the conventional crops and more weeds will be resistant to glyphosate. 184 The District Court then decided that APHIS needs to complete an EIS to comply with NEPA provision. 185 The Court also prohibited the RRA seed distribution and put it back to the regulated status. 186 In 2010, APHIS had appealed this injunction to the US Supreme Court, except for the requirement to conduct an EIS. The Supreme Court afterward set out a decision that the verdict from District Court was lacking justification and there was no sufficient evidence which showing a gene flow from RRA to conventional alfalfa.<sup>187</sup>

Similar to this case, in 2008, also in the same District Court, the Center for Food Safety (CFS) filed a lawsuit against RRSB which has been deregulated by APHIS since 2005. <sup>188</sup> In 2009, the Supreme Court found that genetic contamination could occur which has not been fully considered by APHIS. <sup>189</sup> Two years after that, APHIS has released an environmental assessment followed by a partial deregulation of RSBB which means that the process of seed production remained to be regulated. <sup>190</sup> In 2012, APHIS has finalised the EIS and Plant Pest Risk Assessment (PPRA) to deregulate RRSB based on laboratory data and field analysis handed by Monsanto/KWS, research publication, and other

<sup>180 7</sup> C.F.R. §340.5

<sup>&</sup>lt;sup>181</sup> Bryson, N. (2016). Lessons from the Legal Cases of GM Alfalfa and Sugar Beet Deregulation in the United States, p.103-104. In: *The coexistence of genetically modified, organic and conventional foods: Government policies and market practices.* Kalaitzandonakes, N., Philips, P., Wesseler, J., Smyth, S (ed). Natural resource management and policy, volume 49. New York: Springer, doi:10.1007/978-1-4939-3727-1

<sup>&</sup>lt;sup>182</sup> APHIS. (2007). *Return to Regulated Status of Alfalfa Genetically Engineered for Tolerance to the Herbicide Glyphosate*. Retrieved November 2, 2018 from https://www.aphis.usda.gov/brs/aphisdocs2/04\_11001p\_com.pdf

<sup>&</sup>lt;sup>183</sup> Geertson Seed Farms v. Johanns, 541 F.3d 938, 942 (9th Cir. 2008)

<sup>&</sup>lt;sup>184</sup> Ibid.

<sup>&</sup>lt;sup>185</sup> Geertson Seed Farms v. Johanns, 570 F. 3d 1130, 1133–34 (9th Cir. 2009)

<sup>&</sup>lt;sup>186</sup> Ibid.

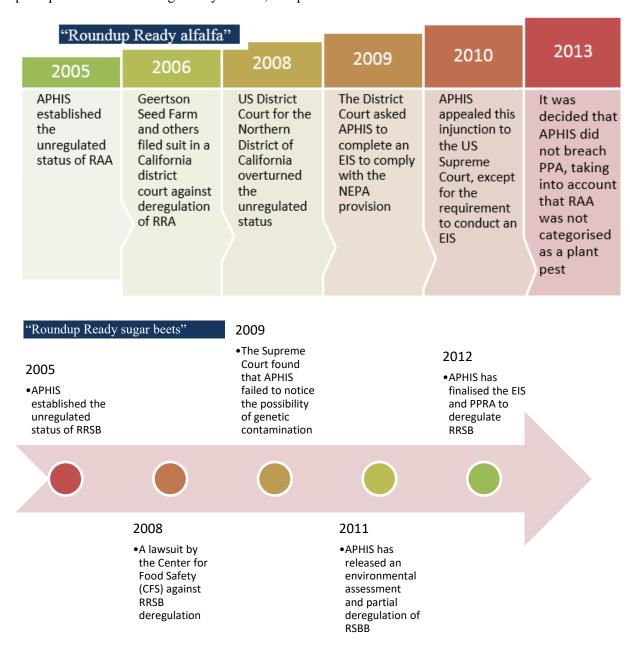
<sup>&</sup>lt;sup>187</sup> Monsanto Co. v. Geertson Seed Farms, 561 U.S. 139 (2010)

<sup>&</sup>lt;sup>188</sup> USDA. (2018). *Roundup Ready Sugar Beet Litigation History*. Retrieved November 3, 2018 from <a href="https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/hot\_topics/sugarbeet/ct\_sugarbeet\_case">https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/hot\_topics/sugarbeet/ct\_sugarbeet\_case</a>

<sup>189</sup> Ibid., 185

<sup>&</sup>lt;sup>190</sup> APHIS. (2011). Monsanto Company and KWS SAAT AG Supplemental Request for Partial Deregulation of Sugar Beet Genetically Engineered to be Tolerant to the Herbicide Glyphosate. Retrieved November 3, 2018 from https://www.aphis.usda.gov/brs/aphisdocs/03\_32301p\_fea.pdf

pertinent information.<sup>191</sup> In 2013, the Ninth Circuit affirmed the district court judgement that APHIS did not breach PPA in considering that RRA was not categorised as a plant pest.<sup>192</sup> From these two cases, it can be drawn that cross pollination could not be considered as a plant pest, and after a non-plant pest status has been given by APHIS, this plant doesn't need to be restricted.<sup>193</sup>



**Figure 2.3.3.4** Timeline of the case studies of "Roundup Ready alfalfa" (RRA) and "Roundup Ready sugar beets (RRSB)

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<sup>&</sup>lt;sup>191</sup> APHIS. (2012). *Determination of Nonregulated Status for H7-1 Sugar Beet*. Retrieved November 3, 2018 from <a href="https://www.aphis.usda.gov/brs/aphisdocs/03">https://www.aphis.usda.gov/brs/aphisdocs/03</a> 32301p feis det.pdf

<sup>&</sup>lt;sup>192</sup> Center for Food Safety v. Vilsack, No. 12-15052 (9th Cir. 2013)

<sup>193</sup> Ibid., 185

#### 2.3.4 LABELING OF GM PRODUCTS

Under the Obama presidency in 2016, the federal labeling bill has been enacted into S.764 which established 'the national bioengineered food standard' (NBFS) as the amendments to the Agricultural Marketing Agreement Act of 1946. Pursuant to paragraph 3 of sec.293 S.764, the GM food which has passed the premarket authorisation by FDA should be treated the same as the non-GM food. To achieve a disclosure standard, the producers shall create an electronic or digital link in the packaging which enabling the consumers to scan or directly go to the web link to gain more information about the engineered products. 194 Another option is that the producers could provide a telephone number to deliver more information by placing statement 'Call for more information' on the packaging. 195 However, lots of critics are coming from the green NGOs and consumers organisations which stated that the consumers would not have time to scan or call the producers and thus, this labeling is not effective to provide sufficient information for buyers. By seeing this condition, this act has been called by the opponents as a DARK act "Deny Americans the Right to Know". On the other hand, the producers side argue that by simply stated engineered information would mislead the consumers, since they do not pose enough information about what GE/GMOs is. An option to disclosure information through the link/phone number provide the consumers a chance to get a contact with the producers directly and apprehend righteous information. This law has also established a provision to allow the organic producers for putting claim "not bioengineered", "non-GMO", and akin, as long as they comply with 7 U.S.C. 6501 to 6524 concerning the organic certification, <sup>196</sup> that may give a win-win solution for the GM and non-GM producers.

To support the implementation of NFBS law, in 2017, the US government has conducted a research regarding the encounter problems that may emerge and hinder the digital disclosure application of GM foods digital labeling. The results reveal that around two-thirds of American citizens own a smartphone, of which 93.6% of the users have an adequate access to the internet and will be able to scan the digital QR code. Furthermore, the government also encouraging a small retailer to put the investment on providing free access of internet to the consumers which could cost around \$10,050, while 97% of national supermarkets have provided this facility. However, a large campaign should be performed by the government and industries to improve the digital literacy and awareness for the

<sup>&</sup>lt;sup>194</sup> S.764—3

<sup>195</sup> Ibid

<sup>&</sup>lt;sup>196</sup> S.764—5

<sup>&</sup>lt;sup>197</sup> USDA. 2017. Study of Electronic or Digital Link Disclosure A Third-Party Evaluation of Challenges Impacting Access to Bioengineered Food Disclosure. Retrieved October 7, 2018 from

https://www.ams.usda.gov/sites/default/files/media/USDADeloitteStudyofElectronicorDigitalDisclosure20170801.pdf

consumers, otherwise the additional cost that have been imposed to producers and retailers would be nugatory.<sup>199</sup>

In a follow up of NFBS law, in 5 April 2018, the Agricultural Marketing Service (AMS), an agency part of the USDA which focuses on the marketing of agricultural products, advocated for a new rule of a GM labelling requirement which would have the entry into force started from January 1, 2020; and January 1, 2021 for small companies.

The proposed rule by AMS chose the word of bioengineered (BE) to be displayed on packaging instead of GMO or GE, in accordance with 7 U.S.C. 1639b, except for foods which do not required labeling as stated in § 101.100. The definition of food in this proposal is slightly different from 21 U.S.C. 321(f), which excluded animal feed from food category. Furthermore, modern technique such as NPBT which do not involve a recombinant DNA<sup>200</sup> and highly refined products which produced from GM crops<sup>201</sup> would also be exempted. AMS also propose to categorize the BE foods based on their adoption, such as canola, maize, soybean, and sugar beet as the highly rated; while the apple, sweet corn, and other fruits will be in the category of the lower adoption rate, considering its value is lower than 85%.<sup>202</sup> The proposed statement on the labeling will also be different for each category. For instance, the highly adopted shall put a declaration of "Bioengineered food" or "Contains a bioengineered food ingredient", while the second one may use "Bioengineered food," "May be bioengineered food," "Contains a bioengineered food ingredient," or "May contain a bioengineered food ingredient."



Figure 2.3.4 The symbols proposed for the new BE foods labeling<sup>204</sup>

This proposed rule has received over 100,000 reactions including from the US producers, consumers, academia, the EU, and several countries. A concern for the small companies which may will not be able to afford this requirement has been considered by the AMS, and thereby, in accordance with the FDA provision, this rule will exempt the small business which their annual income is less than

<sup>199</sup> Ibid

<sup>&</sup>lt;sup>200</sup> Ibid., 21

<sup>&</sup>lt;sup>201</sup> AMS. 2018. *National Bioengineered Food Disclosure Standard*. Retrieved October 7, 2018 from <a href="https://www.federalregister.gov/documents/2018/05/04/2018-09389/national-bioengineered-food-disclosure-standard">https://www.federalregister.gov/documents/2018/05/04/2018-09389/national-bioengineered-food-disclosure-standard</a>

<sup>&</sup>lt;sup>202</sup> Ibid

<sup>203</sup> Ibid

<sup>&</sup>lt;sup>204</sup> Ibid

\$500,000 or the number of their workers are not exceeding 20 people. <sup>205</sup> However, the economists said that the labeling requirement would cause additional cost for retailers to provide more space and storage, which would cost in average \$43 million per year, and more cost have to be borne by farmers and producers for the segregation of GM and non GM products. <sup>206</sup> Last, an interesting comment received from the EU stated that they did not agree with the requirement for the EU exporters to provide a verification document and labeling for the food exported, since it will cause unnecessary cost for the producers, having said that the EU producers do not produce any GM food. <sup>207</sup>

There are typically two generations of GM crops. The first generation has the concerns on improving the input trait by modifying plants with the characteristic of herbicide/pesticide tolerance, while the second one is much focus on elevating the output factors by providing an additional nutritional/health benefit to the final consumers which lead into a better acceptance by consumers. This can be seen from the case of FLAVR SAVR tomato which was highly accepted by consumers, compared to the Bt corn or other GM crops incorporated with the herbicide gene tolerance. In addition, Calgene has voluntarily put the GM labeling on their packaging to get their consumers trust and showing transparency. The consumers own limited knowledge regarding GMOs, while the influence from media has shaped their fears which may influence the outcome on lower acceptance. This situation has created more demand for GM labeling for providing the consumers' rights to know with regards to the ingredients inside their foods.

# 2.3.5 STATE LEGISLATION ADDRESSING GMOs

In 2014, the Vermont law has adopted the first labeling requirement of GMOs in their territory states which was expected to effectively start in July 1, 2016. Many products in the supermarket which are using the genetic engineering techniques in their production need to comply with this provision. Another requirement is that the GM foods would also not allowed to using the word of "natural/naturally made/all natural/other similar words." A huge protests was came from the biotech

<sup>&</sup>lt;sup>205</sup> Ibid

<sup>&</sup>lt;sup>206</sup> Bovay, J., & Alston, J. (2018). GMO food labels in the united states: Economic implications of the new law. *Food Policy*, 78, 14-25.

<sup>&</sup>lt;sup>207</sup> European Union. 2018. *Comments from the European Union regarding notification G/TBT/N/USA/1364*. Retrieved October 7, 2018 from <a href="https://www.regulations.gov/document?D=AMS-TM-17-0050-14033">https://www.regulations.gov/document?D=AMS-TM-17-0050-14033</a>

<sup>&</sup>lt;sup>208</sup> Le Marre, K. N., Witte, C. L., Burkink, T. J., Grünhagen, M., & Wells, G. J. (2007). A second generation of genetically modified food: American versus French perspectives. *Journal of Food Products Marketing*, 13(1), 81-100.

<sup>&</sup>lt;sup>209</sup> Uchtmann, D. (2002). *Regulating Foods Derived from Genetically Engineered Crops*. Retrieved October, 15 2018 from <a href="http://www.farmdoc.illinois.edu/legal/biotech/other\_regulating\_food.pdf">http://www.farmdoc.illinois.edu/legal/biotech/other\_regulating\_food.pdf</a>

<sup>&</sup>lt;sup>210</sup> Lang, J. T., & Hallman, W. K. (2005). Who does the public trust? The case of genetically modified food in the United States. *Risk Analysis: An International Journal*, 25(5), 1241-1252

<sup>&</sup>lt;sup>211</sup> Act. No 120 (H112)

companies and food industries, of which four of the cases ended up in federal court.<sup>212</sup> Obviously, the companies did not want to spend additional cost to create different labeling which only intended for marketed in Vermont. To avoid more confusion and chaos in the market, the USDA Secretary in February 24, 2016 during the public hearing was against this labeling law and has suggested to create a national standardization in federal level.<sup>213</sup> Until finally in July 29, 2016 an NFBS law has been signed by the President of Obama has overturned this rule. Prior to the enactment of NFBS law, several states such as Connecticut and Maine have become the second and the third states which passed the similar labeling law with an additional clause that this law will be enacted when the other states implement the similar law. Unfortunately, other states such as Illinois and Mississippi which propose bill with the similar concerns did not pass the congress. On top of that, a new rule proposed by AMS has created a new possibility of GM labeling just as demanded by the green NGOs and consumers in several states. In Vermont itself, a study conducted by The University of Vermont which involved 7,800 consumers within three years study, showed that a mandatory labeling showing on GM products could reduce the public fear by 19%. 214 Furthermore, a new research has shown that the fear of GMOs may spillover to other biotechnology products, such as for those manufactured by nanotechnology, which cause unnecessary worries and higher risk perception. <sup>215</sup>

#### 2.3.6 CONCLUSIONS

The regulatory framework of GM crops in the US, certainly, is an intricate one. However, after the modernization of the regulatory framework for biotechnology products was conducted in 2017, the coordination between each agency become clearer and quite well directed as summarised in **Table 2.3.5.** The labeling scheme has also changed since the enactment of NFBS law in 2016, and another rule proposed by AMS which has the enforcement date in 2020 will try to accommodate the public which demand more transparency. The NFBS law has also diminished the rules of states agencies in governing GMOs which drive this topic into the authority of federal governments.

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 $<sup>^{212}</sup>$  Orlando, J. 2016. Genetically engineered food labeling. Retrieved October 10, 2018 from  $\underline{\text{https://www.cga.ct.gov/2016/rpt/pdf/2016-R-0031.pdf}}$ 

<sup>&</sup>lt;sup>213</sup> Coalition For Safe Affordable Food. February 24, 2016. USDA Secretary Vilsack Highlights Chaos Vermont's GMO Labeling Law Will Bring. Retrieved October 10, 2018 from <a href="https://www.youtube.com/watch?v=G6LgUcZdpTc">https://www.youtube.com/watch?v=G6LgUcZdpTc</a>

<sup>&</sup>lt;sup>214</sup> UVM. 2018. *Mandatory Labels Reduce GMO Food Fears*. Retrieved October 10, 2018 from https://www.uvm.edu/cals/news/mandatory-labels-reduce-gmo-food-fears

<sup>&</sup>lt;sup>215</sup> Akin, H., Yeo, S., Wirz, C., Scheufele, D., Brossard, D., Xenos, M., & Corley, E. (2018). Are attitudes toward labeling nano products linked to attitudes toward GMO? exploring a potential 'spillover' effect for attitudes toward controversial technologies. *Journal of Responsible Innovation*, 1-25, 1-25. doi:10.1080/23299460.2018.1495026

Table 2.3.5 The Oversight of GM Crops and Relevant Coordination between Agencies

D	and I and	Regulatory Agency Conce	erns	
P	roduct	FDA	USDA-APHIS	EPA
1.	GM crops without pesticidal properties, however contain a novel protein/ substance	The crops will be used for food for human/animal	None	None
	Producer's requirements and responsibilities	Authorisation for food additives	None	None
2.	GM crops with pesticidal properties engineered with a plant pest	The crops will be used for food for human/animal	The plant pest component need to be evaluated	The characteristics of pesticide
	Producer's requirements and responsibilities	Voluntary consultation	<ul> <li>Notification/permit for importation&amp; interstate movement</li> <li>Authorisation for environmental release</li> <li>Environmental assessment or environmental impact statement<sup>216</sup></li> </ul>	-Request a tolerance/tolerance exemption or destroyed all crops which contain pesticidal residue -Experimental use permit <sup>217</sup>
3.	GM crops with pesticidal properties engineered without a plant pest	The crops will be used for food for human/animal	None	The characteristics of pesticide
	Producer's requirements and responsibilities	Voluntary consultation	- Verify its nonregulated status to USDA-APHIS	-Request a tolerance/tolerance exemption or destroyed all crops which contain pesticidal residue -Experimental use permit <sup>218</sup>

<sup>.</sup> 

<sup>&</sup>lt;sup>216</sup> If the GM crops involving new species or organisms or novel modifications that raise new issues (7 CFR § 372.5(d))

<sup>&</sup>lt;sup>217</sup> If the scale of field testing more than 10 acres of land per pest (40 C.F.R. § 172.3)

4. GM crops with herbicide resistant tolerant	The crops will be used for food for human/animal	The plant pest component need to be evaluated	The component of herbicide, <sup>219</sup> not the genetic material inside the GM plants
Producer's requirements and responsibilities	Voluntary consultation	<ul> <li>Notification/permit for importation&amp; interstate movement</li> <li>Authorisation for environmental release</li> <li>Environmental assessment or environmental impact statement<sup>220</sup></li> </ul>	-Request a tolerance/tolerance exemption or destroyed all crops which contain pesticidal residue -Experimental use permit <sup>221</sup>

Source: EPA, 2017 (modified)<sup>222</sup>

<sup>&</sup>lt;sup>218</sup> Ibid

<sup>&</sup>lt;sup>219</sup> In this case this herbicide has been approved by EPA before, however it has not been approved for being used in GM crops

<sup>&</sup>lt;sup>220</sup> Ibid., 218

<sup>&</sup>lt;sup>221</sup> Ibid., 218

<sup>&</sup>lt;sup>222</sup> Ibid., 113



### 3.1 INTRODUCTION

It is obvious that science and biotechnology have already moved very far compared to the very first innovations in the 1980s. The development of GM crops gradually moved from that first generation, which provided many advantages to growers, into the second generation, which benefited consumers directly.<sup>223</sup> Biotech development is moving beyond the realm of agricultural production into different areas, such as human health and consumer satisfaction. For instance, the latest biotech development, so-called transgenic rice, is capable of generating functional HIV-neutralizing proteins that are more potent and cost effective when compared to conventional treatments.<sup>224</sup> To provide the market with more variety, several new biotech fruits have recently been introduced to the US market. These include non-browning Arctic® Apples, Pink-Fleshed 'Rosé' Pineapples, and Cotton Candy® grapes, which offer more flavour and other distinguishing traits when compared to more conventional products, without undermining the safety requirements. However, with the stringent approach adopted in the EU, it seems that these magnificent commodities will not be entering the European market any time soon. There was a similar case in India where the introduction of "golden rice" was so delayed in coming to the market that the delay caused around 1.4 million life-years to be lost because of late adoption of the technology.<sup>225</sup> Conversely, several developed countries with more lenient regulatory approachs toward GMOs, such as Australia, Canada, New Zealand and the USA, quickly approved this product, and will soon be followed by more countries.<sup>226</sup> This asynchronous approval has not only detered the use and adoption of new technology, but also disrupted international trade in cases of adventitious presence that may cause a huge financial loss 227, as illustrated by the example of PR38H20 cases, where the growers have to pay the costs.<sup>228</sup> It is true, though, that the process of risk

<sup>&</sup>lt;sup>223</sup> Heinzerling, L. (2014). U.S. food law (2014 ed.), p.269. Washington: Georgetown University Law Center.

<sup>&</sup>lt;sup>224</sup> Vamvaka, E., Farré, G., Molinos-Albert, L. M., Evans, A., Canela-Xandri, A., Twyman, R. M., ... & Clotet, B. (2018). Unexpected synergistic HIV neutralization by a triple microbicide produced in rice endosperm. *Proceedings of the National Academy of Sciences*, 115(33), E7854-E7862.

<sup>&</sup>lt;sup>225</sup> Wesseler, J., & Zilberman, D. (2014). The economic power of the Golden Rice opposition. Environment and Development Economics, 19(6), 724-742.

<sup>&</sup>lt;sup>226</sup> Dubock, A. (2019). Golden Rice: To Combat Vitamin A Deficiency for Public Health [Online First], *IntechOpen*, DOI: 10.5772/intechopen.84445. Available from: <a href="https://www.intechopen.com/online-first/golden-rice-to-combat-vitamin-a-deficiency-for-public-health">https://www.intechopen.com/online-first/golden-rice-to-combat-vitamin-a-deficiency-for-public-health</a>

<sup>&</sup>lt;sup>227</sup> Anderson, K., Jackson, L. A., & Nielsen, C. P. (2004). *Genetically modified rice adoption: implications for welfare and poverty alleviation*. The World Bank.

<sup>&</sup>lt;sup>228</sup> Wree, P., & Wesseler, J. (2016). Consequences of Adventitious Presence of Non-approved GMOS in Seeds: The Case of Maize Seeds in Germany. In *the Coexistence of Genetically Modified, Organic and Conventional Foods* (pp. 177-183). Springer, New York, NY.

assessment and authorisation needs to be followed, because otherwise we would not be able to turn the invention into a useful product.

# 3.2 COMPARING REGULATORY FRAMEWORK AND IN PRACTICE: STUDY CASE OF GM CROPS RISK ASSESSMENT IN BOTH COUNTRIES

#### 3.2.1 WHO ARE THE PRODUCERS?

As stated in the previous chapter, the process of GM risk assessment is begun by an individual company, which prepares a dossier conforming to the requirements of designated countries as part of the application process to achieve Freedom to Operate (FTO). This process may take up to several years, taking into account the R & D process, financial assessment, and applicable strategies until being successfully introduced in the market. It is widely known that several years ago Monsanto, Syngenta, Dupont, and Bayer were the leading companies in terms of global seed and pesticide production. Process Recently, these companies have followed a new strategy to merge and expand their global business. DuPont and Dow Chemical merged in 2017, establishing Corteva Agriscience their agricultural division. Similarly, ChemChina has purchased Syngenta with the aim of expanding their niche market and increasing their global position against other giant biotech companies. Most recently, a merger between Monsanto and Bayer with a fantastic value of US\$ 66 billion 231 completed the biotech integration saga, the goal being to sustain their business growth. Those newly transformed companies are projected to own over sixty percent of the seeds and crop protection products in the world market.

# 3.2.2 THE GM CROPS IN THE EU AND THE US

In the EU, there are six types of crops which have been approved by the EC, namely, cotton, maize, soybean, oilseed rape, sugar beet, and swede rape. However, the last one has been withdrawn from the market, because there was no intention from the producer to renew the authorisation. Most of the GM

<sup>&</sup>lt;sup>229</sup> Moldenhauer, H and Hirtz, S. (2017). *Monsanto and Co: From seven to four – growing by shrinking*. Retrieved at April 22, 2019 from <a href="https://www.boell.de/en/2017/10/31/monsanto-and-co-from-seven-to-four-growing-by-shrinking?dimension1=ds">https://www.boell.de/en/2017/10/31/monsanto-and-co-from-seven-to-four-growing-by-shrinking?dimension1=ds</a> agrifoodatlas

<sup>&</sup>lt;sup>230</sup> Patton, D. (2018). *China-owned Syngenta plots growth in challenging home market*. Retrieved at April 22, 2019 from <a href="https://www.reuters.com/article/us-china-syngenta/china-owned-syngenta-plots-growth-in-challenging-home-market-idUSKBN1KE1B3">https://www.reuters.com/article/us-china-syngenta/china-owned-syngenta-plots-growth-in-challenging-home-market-idUSKBN1KE1B3</a>

<sup>&</sup>lt;sup>231</sup> Reuters. (2017). *Bayer, Monsanto start* \$2.5 *billion asset sale to get merger clearance: sources*. Retrieved at April 26, 2019 from https://www.reuters.com/article/us-monsanto-m-a-bayer-idUSKBN16G1PB

<sup>&</sup>lt;sup>232</sup> European Commission. (2018). *Mergers: Commission clear acquisition of parts of Bayer's crop science business by BASF, subject to conditions.* Retrieved April 22, 2019 from http://europa.eu/rapid/press-release\_IP-18-3622\_en.htm

<sup>&</sup>lt;sup>233</sup> Moldenhauer, H and Hirtz, S. (2017). *Monsanto and Co: From seven to four – growing by shrinking*. Retrieved at April 22, 2019 from <a href="https://www.boell.de/en/2017/10/31/monsanto-and-co-from-seven-to-four-growing-by-shrinking?dimension1=ds\_agrifoodatlas">https://www.boell.de/en/2017/10/31/monsanto-and-co-from-seven-to-four-growing-by-shrinking?dimension1=ds\_agrifoodatlas</a>

crops are authorised for food, feed, and import. MON810 and Amflora are examples of the few GM plants that have been grown in EU territory. Several countries in the EU have a history of GM crops grown in the past. Unfortunately, GM cultivation has most often been greeted by hostile political action and painful rejection by the other Member States. Spain and Portugal are the only countries that still grow the MON 810. In other countries, such as Czech and Slovakia, farmers have stopped planting GM crops because of the meticulous reporting requirements and the general hassle in selling their products.<sup>234</sup>

In the US, GM crops cultivations are dominated by maize, soybean, alfalfa, cotton, and canola which amount to 40% of the global market share for biotech crop and are valued at US\$80.3 billion over the last ten years.<sup>235</sup> Approximately three-quarter of all prepackaged food sold in US retail and wholesale chains may come from biotech crops.<sup>236</sup>

#### 3.2.3 COMPARATIVE ANALYSIS

One interesting finding when delving into the regulatory framework is that the risk assessment principles in the US and the EU have some similarities. For example, the first and second steps in the EU are similar to the concept of substantial equivalence in the US, which were developed by the OECD<sup>237</sup> and the joint report of WHO/FAO.<sup>238</sup> After the concept had been formulated, the member countries, including the EU and US, have adopted this concept into their policies. However, this report has yielded various interpretations that differ in each country, which has led to accusations of protectionism.<sup>239</sup> The original concept, rooted in the substantial equivalence principle, means that whenever the components of GM foods are similar to non GMOs, these two categories shall receive the same treatment.

Although it looks simple, the applications of this concept are significantly different, with each country adopting a different approach. Some researchers consider that the EU is adopting a process-based concept, while the US relies on the product-based approach, or perhaps a hybrid system that combines both.<sup>240</sup> While the current molecular characterisation studies are based upon PCR based approaches, some scholars suggested that molecular profiling through omics is important when conducting

<sup>236</sup> Heinzerling, L. (2014). U.S. food law (2014 ed.), p.226. Washington: Georgetown University Law Center.

<sup>&</sup>lt;sup>234</sup> ISAAA. (2017). Global Status of Commercialized Biotech/GM Crops in 2017: Biotech Crop Adoption Surges as Economic Benefits Accumulate in 22 Years. Retrieved October 12, 2018, from http://www.isaaa.org/resources/publications/briefs/53/download/isaaa-brief-53-2017.pdf

<sup>235</sup> Ibid

<sup>&</sup>lt;sup>237</sup> Ibid 158

<sup>&</sup>lt;sup>238</sup> WHO. (1991). Strategies for assessing the safety of foods produced by biotechnology. Retrieved October 18, 2018 from <a href="http://apps.who.int/iris/bitstream/handle/10665/41465/9241561459-eng.pdf?sequence=1&isAllowed=y">http://apps.who.int/iris/bitstream/handle/10665/41465/9241561459-eng.pdf?sequence=1&isAllowed=y</a>

<sup>&</sup>lt;sup>239</sup> Kok, E. J., & Kuiper, H. A. (2003). Comparative safety assessment for biotech crops. *TRENDS in Biotechnology*, 21(10), 439-444.

<sup>&</sup>lt;sup>240</sup> Marchant, G. E., & Stevens, Y. A. (2015). A new window of opportunity to reject process-based biotechnology regulation. *GM crops & food*, 6(4), 233-242.

molecular characterisation and assessing the susbtantial equivalence between the GM and the non GM product. <sup>241</sup> Omics can be defined as "the collective technologies used to explore the roles, relationships, and actions of the various types of molecules that make up the cells of an organism." <sup>242</sup> Omics is not only useful in molecular characterisation, this study may also be a powerful tool for use in other research areas, such as toxicological assessment. <sup>243</sup> Currently, EFSA is investigating omics in support of future GM risk assessment strategies. <sup>244</sup> There are, however, many critics in the industry who believe that the technology is not ready yet. It is also important to differentiate between scientific curiosity and the fundamental goal of GM risk assessment, which is to ensure that the product does not pose any risk to human and animal health, or the environment. It seems to the critics that applying omics to the entire process would be unnecessary and unlikely to help to achieve the paramount goal of risk assessment, instead just making the application process more costly and time consuming.

Table 3.2.3.1 The Summary of Risk Assessment Principles in the EU and US

	Step 1	Step 2	Step 3	Step 4
The EU	Molecular characterisation of	Comparative analysis of compositional,	Safety assessment for humans and	<b>Environmental impact</b>
	the GM plant	phenotypic and	animals	
		agronomic properties		
Focused	The structure and	The selection of the	Toxicology testing	The potential risk to the
elements	manifestation of the	conventional	for every new	environment (short term
	embedded gene, the	counterpart and	substance and	and long term), control
	gene stability, the	comparator, take heed	identifying the	and emergency plan,
	gene transfer (for	of the composition,	allergen compounds	stack plant
	e.r.a)	phenotypic, and		transformation
		agronomic features		
The US	Substantial	Toxicity and nutrient	Allergenicity	Environmental impact
	equivalence	composition		
Focused	The introduction of	The nutrient	The substance	The potential of
elements	the structure and	component and	(allergen) which	becoming a plant pest,

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<sup>&</sup>lt;sup>241</sup> Heinemann, J. A., Kurenbach, B., & Quist, D. (2011). Molecular profiling—a tool for addressing emerging gaps in the comparative risk assessment of GMOs. *Environment international*, *37*(7), 1285-1293.

<sup>&</sup>lt;sup>242</sup> AltTox. (2014). *Omics, bioinformatics, computational biology*. Retrieved July 22, 2019 from <a href="http://alttox.org/mapp/emerging-technologies/omics-bioinformatics-computational-biology/">http://alttox.org/mapp/emerging-technologies/omics-bioinformatics-computational-biology/</a>

<sup>&</sup>lt;sup>243</sup> Gruiz, K., Meggyes, T., & Fenyvesi, E. (Eds.). (2014). *Engineering tools for environmental risk management* (Vol. 1, environmental deterioration and contamination - problems and their management /, Balkema book), p.14. Leiden, The Netherlands: CRC Press/Balkema.

<sup>&</sup>lt;sup>244</sup> Lanzoni, A. (2019). GMO Risk Assessment Future perspectives. Retrieved July 22, 2019 from <a href="https://www.efsa.europa.eu/sites/default/files/event/6.%20Anna%20Lanzoni">https://www.efsa.europa.eu/sites/default/files/event/6.%20Anna%20Lanzoni</a> %20stakeholder academia 2019 final.pdf

manifestation of bioavailability, the considered to be put the gene expressions, the genetic material, the level of toxicant and in labeling interaction with the identification of its effect environment (gene traditional transfer) counterpart, metabolic pathway, the stability of the new trait

The third step of the EU risk assessment process (safety assessment for humans and animals) is identical to the steps for the toxicity and nutrient composition of GM plants, as well as the allergenicity testing in the US. All of these procedures are important for the safety evaluation to protect human and animal health. Many aspects are considered, including toxicity, nutrient content, and allergenicity. There is some debate over whether the regulatory approach should be based on "proof of safety" or "proof of harm" when it comes to this step. <sup>245</sup> The debate surrounding the necessity of animal study has been addressed in Chapter II. As it stands, this section would not normally propose a new study requirement. It will refer to the results of step 1 and step 2.

Lastly, the environmental risk assessment conducted by the EFSA and USDA-APHIS is considered to be the most stringent process when compared to the prior methods, leading to the highest rejection rate compared to the others. At the beginning, the USDA categorised all GM plants as being plant pests under the PPA, which resulted in a huge cost and significant delay. Since 2003, APHIS has faced several lawsuits from the NGOs based on infringements of the NEPA's provisions. The GM crops that will go on to field trials shall follow the process of notification by making a permit application. Currently, the APHIS is tightening its monitoring system of GM wheat field trials after discovering that GM wheat (MON 71300 and MON 71800) was being grown in Washington State without any permit. Although the FDA has concluded that the GM wheat is as safe as the conventional food, there is currently neither sale nor commercial production of GM wheat in the US.

<sup>&</sup>lt;sup>245</sup> Kuzma, J., & Haase, R. (2012). Safety Assessment of Genetically Engineered Foods: US Policy & Current Science. *Safety*.

<sup>&</sup>lt;sup>246</sup> Marchant, G. E., & Stevens, Y. A. (2015). A new window of opportunity to reject process-based biotechnology regulation. *GM crops & food*, 6(4), 233-242.

<sup>&</sup>lt;sup>247</sup> McGinnis, E. E., Meyer, M. H., & Smith, A. G. (2012). Analysis of US genetically engineered crop regulation and litigation. *Crop science*, 52(3), 991-1002.

<sup>&</sup>lt;sup>248</sup> APHIS. (2019). *USDA Investigating Detection of Genetically Engineered (GE) Wheat in Washington State*. Retrieved July 25, 2019 from https://www.aphis.usda.gov/aphis/newsroom/stakeholder-info/sa\_by\_date/2019/sa-6/ge-wheat

<sup>&</sup>lt;sup>249</sup> APHIS. (2019). APHIS Provides Update on Detection of Genetically Engineered (GE) Wheat. Retrieved July 25, 2019 from https://www.aphis.usda.gov/aphis/newsroom/stakeholder-info/sa\_by\_date/2019/sa-07/ge-wheat

If the producers would like to achieve full commercialisation and the permission to grow the crop anywhere in the US, they need to apply for a more complex process through a system called complete deregulation. APHIS will then perform an environmental assessment to establish a Finding of No Significant Impact (FONSI).<sup>250</sup> Otherwise, if any significant issue emerges, APHIS may start the process of environmental risk assessment<sup>251</sup> which will require the applicants to pay an enormous price and wait for a very long time.<sup>252</sup>

In the EU, GM crops intended for cultivation must follow the complete environmental risk assessment process. Last year, a new Commission Directive (EU) 2018/350 amending Directive 2001/18/EC of the European Parliament and of the Council about the environmental risk assessment of genetically modified organisms was introduced to implement the technical progress arising from the experience obtained in prior environmental risk assessments. However, at the moment there is no incentive for companies to apply for GM cultivation in the EU, considering the low chance to get the approval and the possibility of being banned by the Member States.

Table 3.2.3.2 Number of Dossiers Retrieved from the EFSA and the US agencies

EFSA	US FDA	APHIS-FDA	EPA
43	6	0	21

The distinction between the risk assessment requirements in the EU and the US can also be identified in the dossiers submitted by the companies. In the US, the summaries of the applications can be obtained from the agency's website and more detailed information can be requested from FOIA. These findings are summarised in **Table 3.2.3.3**. In most cases, the company doesn't distinguish between the requirement in the regulation and guideline published by the agency. As long as the guideline is reasonable and in line with the applicable regulations, the company so far has followed it diligently. It is important to keep in mind that in the EU especially, each GMO requires certain studies and there are different protocols to follow, and thus, each submission can be considered to be unique and will be treated using a case-by-case approach.<sup>253</sup> The EU also differentiates between crops that are single and stacks, which make any generalisations become more complicated. This could be considered to be a limitation of this study, because this thesis seeks to identify the general patterns and protocols between each of the dossiers, without addressing whether these may be applied in, or be irrelevant to, certain cases of application.

<sup>250 40</sup> CFR § 1501.4

<sup>251 40</sup> CFR § 1501.7

<sup>&</sup>lt;sup>252</sup> McGinnis, E. E., Meyer, M. H., & Smith, A. G. (2012). Analysis of US genetically engineered crop regulation and litigation. *Crop science*, 52(3), 991-1002.

<sup>&</sup>lt;sup>253</sup> EFSA. (2019). GMO. Retrieved May 26, 2019, from https://www.efsa.europa.eu/en/topics/topic/gmo

Table 3.2.3.3 List of Data Requirements for GM Crops Risk Assessment in the EU and US

Data Required	The EU	The US	The US		
		FDA	APHIS	EPA	
Description of Product					
- Summary	v	v	v	v	
- Product Background	v	V	v	v	
2. The Host Plant	•		•	·	
<ul> <li>Safety Assessment of New Varieties: The Host Plant</li> </ul>	V	v	v	-	
3. The Donor(s)					
<ul> <li>Safety Assessment of New Varieties: The Donor(s)</li> </ul>	V	V	-	V	
4. Description of the Genetic Modification					
<ul> <li>Substances Introduced into the Host Plant from the Donor(s)</li> </ul>	V	v	v	V	
5. Characterization of the Genetic Modification	v	v	v	v	
- Safety Assessment of Expressed Products	v	v	v	-	
Agronomic, Phenotypic, and Environmental Interactions	v	-	V	<b>v</b> <sup>254</sup>	
7. Composition Assessment for Food/Feed Safety	V	V	V	<b>v</b> <sup>255</sup>	
90-day feeding studies	<b>v</b> <sup>256</sup>	-	-	-	
28-day toxicity study	V	-	-	-	
8. Environmental Consequences <sup>257</sup>	-	-	v	v	
- Observation for NTOs	_	-	v	-	
- NTOs for PIPs	-	-	-	v	
9. US Agronomic Practices	-	v	-	-	

# 3.3 THE RATIONALE BEHIND DIFFERENT APPROACHES

# 3.3.1. DEFINING THE RISK

Scientists and politicians often talk about risks from two different perspectives. One is the context of risks that can pose a threat to human health and environment, and another type of risk is related to

<sup>&</sup>lt;sup>254</sup> Only for a new crop or an existing crop with the change on its MRL, information about herbicide residue must be included

<sup>&</sup>lt;sup>255</sup> Required for first generation PIPs

<sup>&</sup>lt;sup>256</sup> Mandatory for a single event, and case by case for stack events

<sup>&</sup>lt;sup>257</sup> In the EU, this part is applicable for the GM plant cultivation

socio-economic perspectives.<sup>258</sup> Risk can also be divided into risks that show a direct linkage of causation, as opposed to systemic risks that arise as the result of a series of events.<sup>259</sup> To minimise this risk, the respective agency will evaluate the safety assessment of GMOs during the process of risk assessment. In addition, far before this process takes place, the company will certainly have assessed every possible risk that may occur to ensure the safety and efficacy of the product.<sup>260</sup> Even so, the profound and comprehensive safety assessments of GMOs did not change the public opinion about this issue.<sup>261,262</sup> It seems that the risks associated with GMOs relate not only to the scientific aspects, but also contain a huge public concern as illustrated in **Figure 3.3.1**. Certain food crises in the late 1990s must have deeply affected EU citizens in their perception of the risks, while at the same time showing the incapability of the government to handle such a crisis.<sup>263</sup> The unpopular shipment of GM maize from US has also caused a public outcry and a great deal of media attention.<sup>264</sup> Any novelty product, especially GMOs, since then has been subjected to a stringent regulatory approach in the EU legislature, casting a shadow over the existence of precautionary principles.<sup>265</sup>

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<sup>&</sup>lt;sup>258</sup>Sparrow P.A. (2009) GM Risk Assessment. In: Jones H., Shewry P. (eds) Transgenic Wheat, Barley and Oats. *Methods in Molecular Biology* TM (*Methods and Protocols*), vol 478. Humana Press

<sup>&</sup>lt;sup>259</sup> Breckling, B. (2011). Spatial Ecology and an Integrative Framework. In *New challenges in risk assessment of Genetically Modified Plants –Establishing a research programme aiming for integrative risk assessment*. Retrieved April 22, 2019 from <a href="http://pure.au.dk/portal/files/128938241/Integrated Risk Assessment of GMO CPH Dec 2011 Presentations.pdf">http://pure.au.dk/portal/files/128938241/Integrated Risk Assessment of GMO CPH Dec 2011 Presentations.pdf</a>

<sup>&</sup>lt;sup>260</sup> Ibid

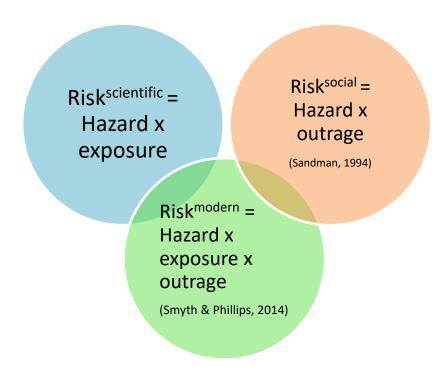
<sup>&</sup>lt;sup>261</sup> Chilebio. (2014). Declaraciones científicas que reconocen los beneficios y la seguridad de los cultivos transgénicos para los consumidores, el medio ambiente y los agricultores. Retrieved April 22, 2019 from <a href="https://www.chilebio.cl/documentos/datos\_chileb.pdf">https://www.chilebio.cl/documentos/datos\_chileb.pdf</a>

<sup>&</sup>lt;sup>262</sup> Pellegrino, E., Bedini, S., Nuti, M., & Ercoli, L. (2018). Impact of genetically engineered maize on agronomic, environmental and toxicological traits: a meta-analysis of 21 years of field data. *Scientific reports*, 8(1), 3113.

<sup>&</sup>lt;sup>263</sup> Vogel, D. (2001). *The new politics of risk regulation in Europe*. London School of Economics and Political Science, LSE Library.

<sup>&</sup>lt;sup>264</sup> Lynch, D., & Vogel, D. (2001). The regulation of GMOs in Europe and the United States: A case-study of contemporary European regulatory politics. *Council on Foreign Relations*, 5.

<sup>&</sup>lt;sup>265</sup> Lucht, J. (2015). Public acceptance of plant biotechnology and GM crops. Viruses, 7(8), 4254-4281.



Source: Sandman, 1994<sup>266</sup>, Smyth & Phillips, 2014<sup>267</sup>

Figure 3.3.1 Risk Definitions

#### 3.3.2 THE ROLE OF PREVENTIVE AND PRECAUTIONARY MEASURES

In addressing GMOs, the EU is relying on the precautionary principle, both for market authorisation and for the introduction of GMOs into the environment.<sup>268</sup> Both situations are linked to Article 1 as the objective of the Cartagena Protocol on Biosafety (CPB) as follows:

"In accordance with the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development, the objective of this Protocol is to contribute to ensuring an adequate level of protection . . . of living modified organisms resulting from modern biotechnology that may have adverse effects on . . . biological diversity, taking also into account risks to human health, and specifically focusing on trans boundary movements." The precautionary measure was adopted from the principle 2 of the Rio Declaration—the prevention in international law on environment and development. In case where severe damage could happen, the prevention principle could take a role as a precautionary measure to avoid any further damage. <sup>269</sup>

Without considering its complexity, the precautionary principle, in short, is developed through the ideas that "prevention is better than cure" and the "polluter pays." These principles consider the

<sup>&</sup>lt;sup>266</sup> Sandman P. (1994). Mass media and environmental risk: Seven principles. *Risk*; 5:251-60.

<sup>&</sup>lt;sup>267</sup> Smyth, S. J., & Phillips, P. W. (2014). Risk, regulation and biotechnology: the case of GM crops. *GM crops & food*, 5(3), 170-177.

<sup>&</sup>lt;sup>268</sup> Art 1 Directive 2001/18/EC

THE I DIRECTIVE 2001/10/EC

<sup>&</sup>lt;sup>269</sup> de Sadeleer, Nicolas. (2002). *Environmental Principles – From Political Slogans to Legal Rules*. Oxford University Press

fragility of nature and prioritize the victim over the party that may get any benefit from it.<sup>270</sup> This concept is frequently applied when serious threats may arise, and sometimes economic freedom becomes the trade-off.<sup>271</sup> The precautionary principle is also mentioned in Article 191(2) TFEU, which emphasizes the high level of protection that shall be based on this principle and on the preventative principle, despite the diverse situation in the EU. There is no definition or secondary legislation that provides a further explanation. However, paragraph 99 on the BSE court case provides an argument that "Where there is uncertainty as to the existence or extent of risks to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent."<sup>272</sup>

This idea is strengthened by the judge interpretation of Case T-13/99 paragraph 146: "The precautionary principle can therefore apply only in situations in which there is a risk, notably to human health, which, although it is not founded on mere hypotheses that have not been scientifically confirmed, has not yet been fully demonstrated."<sup>273</sup>

As the main function of the precautionary principle is use as a risk reduction tool, the process of risk management often uses this protocol to address scientific and political uncertainties.<sup>274</sup> It is up to the relevant authorities to decide the level of protection, considering the public concerns shaped in the Union.<sup>275</sup> The precautionary principle on GMOs has undergone a transformation from ex post control into ex ante control.<sup>276</sup> Although there has not been any evidence showing that GMOs pose a risk to human and animal health, and/or to the environment, some scholars have suggested that unacceptable hazards, including to societal values, could invoke this provision.<sup>277</sup> This process nevertheless shall be based on the concepts of proportionality and non-discrimination, and on other crucial principles, with the ultimate goal of choosing an appropriate level of protection in the light of scientific data.<sup>278</sup> Thus, if there is sufficient data and measurable risk, the assessment shall be based on the preventive method instead of the precautionary approach. Unless there is adequate explanation, however, the consistency

<sup>&</sup>lt;sup>270</sup> Mayer, S., & Stirling, A. (2002). Finding a precautionary approach to technological developments—lessons for the evaluation of GM crops. *Journal of Agricultural and Environmental Ethics*, *15*(1), 57-71.

<sup>&</sup>lt;sup>271</sup> Ekardt, F., Wieding, J., & Zorn, A. (2018). Paris Agreement, Precautionary Principle and Human Rights: Zero Emissions in Two Decades? *Sustainability*, *10*(8), 2812.

<sup>&</sup>lt;sup>272</sup> Judgment of the Court of 5 May 1998. *United Kingdom of Great Britain and Northern Ireland v Commission of the European Communities*. Agriculture - Animal health - Emergency measures against bovine spongiform encephalopathy - 'Mad cow disease'. Case C-180/96. European Court Reports 1998 I-02265

<sup>&</sup>lt;sup>273</sup> Case T-13/99. Pfizer Animal Health SA v. Council of the European Union. European Court Reports 2002 II-03305

<sup>&</sup>lt;sup>274</sup> Sharma, A. (2017). Precaution and post-caution in the Paris Agreement: adaptation, loss and damage and finance. *Climate Policy*, 17(1), 33-47.

<sup>&</sup>lt;sup>275</sup> European Commission. (2000). *Communication from The Commission on the precautionary principle*. Brussels, 2.2.2000 COM (2000) 1 final

<sup>&</sup>lt;sup>276</sup> de Sadeleer, Nicolas. (2002). *Environmental Principles – From Political Slogans to Legal Rules*. Oxford: Oxford University Press

<sup>&</sup>lt;sup>277</sup> Dessai, S., & van der Sluijs, J. P. (2007). *Uncertainty and climate change adaptation: a scoping study* (Vol. 2007). Copernicus Institute for Sustainable Development and Innovation, Department of Science Technology and Society.

<sup>&</sup>lt;sup>278</sup> Ibid., 269

between these two concepts and applications will sometimes become confusing in the EU.<sup>279</sup> In response to this, some scholars hold the view that the precautionary principle is part of the government's aversion to taking protective measures in uncertain situation.<sup>280</sup> There are always some potential errors in any human system, and the type 2 error, rejecting a safe product, is often neglected.<sup>281</sup> For people with insufficient knowledge, risks would be hard to be evaluate objectively.<sup>282</sup> In the end, it is up to the risk managers to set the level of protection and invoke the precautionary principle. That will eventually influence the process of rigorous safety assessment by creating a more risk averse policy to defend public interests.<sup>283</sup>

Similarly, the US also applies the precautionary approach in fields related to environmental policies. This has generally been stricter than that applied by the EU, especially in the period between the 1960s till the mid of 1980s, when American society was more reluctant to accept risks. However, GMO regulation in the US has followed a different path, relying on an assumption that biotechnology products are similar to traditional seeds, and thus a product based system has been adopted. One interesting study that identified a list of almost 3000 risks that existed in the two countries found that the various trends among the risks showed that both countries have various areas with more, less, or equal precaution. From this study it can be seen that the US has greater precautions relating to alcohol, tobacco, pollution, and accident, while the EU has more precautions related to energy production, food, agriculture, and human health.

Back to the EU decision making process, public concerns toward GMOs have become the priority consideration, and political reasons to authorise or reject the product, and to decide the strictness of the regulation, are generally applied.<sup>288,289</sup> If we differentiate between "GMO familiarity" and the global

<sup>&</sup>lt;sup>279</sup> Garnett, K., & Parsons, D. J. (2017). Multi-Case Review of the Application of the Precautionary Principle in European Union Law and Case Law. *Risk Analysis*, 37(3), 502-516.

<sup>&</sup>lt;sup>280</sup> Bergkamp, L and Hanekamp, J. (2018). European Food Law and the Precautionary Principle: Paradoxical Effects of the EU's Precautionary Food Policies p.234. In: *Regulating and managing food safety in the EU: A legal-economic perspective*. Bremmers, H and Purnhagen, K (ed). Economic analysis of law in European legal scholarship, volume 6. Cham, Switzerland: Springer.

<sup>&</sup>lt;sup>281</sup> Smyth, S. J., & Phillips, P. W. (2014). Risk, regulation and biotechnology: the case of GM crops. *GM crops & food*, 5(3), 170-177.

<sup>&</sup>lt;sup>282</sup> Zander J. *The Application of the Precautionary Principle in Practice: Comparative Dimensions*, p.12. Cambridge: Cambridge University Press, 2010.

 $<sup>^{283}</sup>$  Jordan, A., & O'Riordan, T. (1995). The precautionary principle in UK environmental law and policy. In  $\it UK$   $\it Environmental Policy in the 1990s$  (pp. 57-84). Palgrave Macmillan, London.

<sup>&</sup>lt;sup>284</sup> Vogel, D. (2001). *Ships Passing in the Night: The Changing Politics of Risk Regulation in Europe and the United States* (No. 16). European University Institute (EUI), Robert Schuman Centre of Advanced Studies (RSCAS).

<sup>&</sup>lt;sup>285</sup> Ibid

<sup>&</sup>lt;sup>286</sup> Hammitt, J. K., Wiener, J. B., Swedlow, B., Kall, D., & Zhou, Z. (2005). Precautionary regulation in Europe and the United States: a quantitative comparison. *Risk Analysis: An International Journal*, 25(5), 1215-1228.

<sup>287</sup> **Thi**d

<sup>&</sup>lt;sup>288</sup> Herring, R. J. (2008). Opposition to transgenic technologies: ideology, interests and collective action frames. *Nature Reviews Genetics*, 9(6), 458.

knowledge base, the understanding of GMOs is still weak.<sup>290</sup> Taking the example of US consumers, the majority of whom favour GM labelling, 54% admitted to have little or low knowledge about GMOs and more than 50% believed fallacies like the perception that GM chickens and tomatoes are sold in the supermarket.<sup>291</sup> While in the EU, the result from the Eurobaromater published in June, 2019 showed that people now have fewer concerns about GMOs when compared to almost ten years ago.<sup>292</sup> The latest survey revealed that 60% of the respondents have heard about GMOs, and only 27% are concerned about GM foods. This is lower than the concern for antibiotic, hormone or steroid residues in meat (44%), pesticide residues in food (39%), and food hygiene (32%).<sup>293</sup> These findings will no doubt help the policy makers to reevaluate the public's fears of the risks related to GMOs as shown in social constructs.

The implication of this complex situation is that the GM authorisation procedure in the EU has become more lengthy and stricter. This has caused asynchronous approval, meaning that some GM crops have been approved in several countries but not in the EU.<sup>294</sup> This event will affect global trade, because there will be more rejections on the borders in cases of low adventitious presence.<sup>295</sup> Potential markets between the EU and trading partners are unlikely to grow,<sup>296</sup> and most importantly, the vast majority of innovative products will be arrested in the development stage without having a chance to enter the market. <sup>297</sup> Combined with the negative framing of GMOs as 'unnatural' and 'anti-developmental', this complex situation has shaped the negative perceptions of consumers and lowered interest in buying these kinds of products.<sup>298</sup> The same pressure is also experienced by food retailers,

<sup>&</sup>lt;sup>289</sup> Bonny, S. (2003). Why are most Europeans opposed to GMOs? Factors explaining rejection in France and Europe. *Electronic journal of biotechnology*, 6(1), 7-8.

<sup>&</sup>lt;sup>290</sup> Wunderlich, S., & Gatto, K. A. (2015). Consumer perception of genetically modified organisms and sources of information. *Advances in Nutrition*, 6(6), 842-851.

<sup>&</sup>lt;sup>291</sup> Hallman WK, Cuite CL, Morin XK. (2013). *Working Paper 2013–1: Public perceptions of labeling genetically modified foods*. New Brunswick (NJ): Rutgers, the State University of New Jersey, School of Environmental and Biological Sciences. Retrieved July 25, 2019 from <a href="http://humeco.rutgers.edu/documents">http://humeco.rutgers.edu/documents</a> <a href="https://humeco.rutgers.edu/documents">PDF/news/GMlabelingperceptions.pdf</a>

<sup>&</sup>lt;sup>292</sup> EFSA. (2019). Europeans on today's food issues: new EU-wide survey comes out on first World Food Safety Day. Retrieved July 25, 2019 from https://www.efsa.europa.eu/en/press/news/190607

 $<sup>^{293}</sup>$  Eurobarometer. (2019). Special Eurobarometer - April 2019 "Food safety in the EU". Retrieved July 25, 2019 from <a href="https://www.efsa.europa.eu/sites/default/files/corporate">https://www.efsa.europa.eu/sites/default/files/corporate</a> publications/files/Eurobarometer2019 Food-safety-in-the-EU Full-report.pdf

<sup>&</sup>lt;sup>294</sup> Ibid

<sup>&</sup>lt;sup>295</sup> Grossman, M.R. (2018). Agricultural Biotechnology: Regulation in the United States and the European Union p.333. In: *Regulating and managing food safety in the EU: A legal-economic perspective.* Bremmers, H and Purnhagen, K (ed). Economic analysis of law in European legal scholarship, volume 6. Cham, Switzerland: Springer.

<sup>&</sup>lt;sup>296</sup> DG Agri Report. (2007). Economic Impact of Unapproved GMOs on EU Feed Imports and Livestock Production. Retrieved April 22, 2019 from

https://ec.europa.eu/agriculture/sites/agriculture/files/publi/reports/gmo/economic impact unapproved gmos en.pdf

<sup>&</sup>lt;sup>297</sup> Menrad, K., & Blind, K. (2006). 10 The Impact of Regulation on the Development of New Products in the Food Industry. *International Trade and Policies for Genetically Modified Products*, 110.

<sup>&</sup>lt;sup>298</sup> Herring, R. J. (2008). Opposition to transgenic technologies: ideology, interests and collective action frames. *Nature Reviews Genetics*, 9(6), 458.

who are unwilling to sell any GM product as fear comes with the full glare of publicity and the danger of boycotts from green NGOs.<sup>299</sup>

Inside the EU organisation, 'culture consensus' is highly reflected in Council votes on GMOs, shaped by public opinion and political stake, together with the multifaceted interests of the Member States.<sup>300,301</sup> In general, the political attitudes of Member States toward GMOs are divided into three different categories, namely the adopters, the conflicted, and the opposed, as depicted in **Figure 3.3.2.**<sup>302</sup> Spain, Portugal, the Czech Republic, Slovakia, and Romania are the examples of the MSs that are pleased to adopt modern biotechnology.<sup>303</sup> The other MSs could have several challenges coming from the green NGOs' resistance and consumers who are sceptical about GM foods and thus have influenced the MS's voting attitude.<sup>304</sup> However, this general classification is quite flexible, as this is only based on the public opinion coming mostly from farmers and consumers.<sup>305</sup>

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<sup>&</sup>lt;sup>299</sup> Kettnaker, V. (2001). The European conflict over genetically engineered crops, 1995-1997. *Contentious Europeans*, 205-230.

<sup>&</sup>lt;sup>300</sup> Vigani, M., & Olper, A. (2015). Patterns and Determinants of GMO Regulations: An Overview of Recent Evidence. *AgBioForum*, 18(1), 44-54.

<sup>&</sup>lt;sup>301</sup> Mühlböck, M., & Tosun, J. (2018). Responsiveness to different national interests: Voting behaviour on genetically modified organisms in the council of the European Union. *JCMS: Journal of Common Market Studies*, 56(2), 385-402.

<sup>&</sup>lt;sup>302</sup> Dunwell, J. M. (2014). Genetically modified (GM) crops: European and transatlantic divisions. *Molecular plant pathology*, *15*(2), 119-121.

<sup>&</sup>lt;sup>303</sup> Lucht, J. (2015). Public acceptance of plant biotechnology and GM crops. Viruses, 7(8), 4254-4281.

<sup>&</sup>lt;sup>304</sup> Nausch, H., Sautter, C., Broer, I., & Schmidt, K. (2015). Public funded field trials with transgenic plants in Europe: A comparison between Germany and Switzerland. *Current opinion in biotechnology*, 32, 171-178.

<sup>&</sup>lt;sup>305</sup> ISAAA. (2017). *Global Status of Commercialized Biotech/GM Crops in 2017: Biotech Crop Adoption Surges as Economic Benefits Accumulate in 22 Years*. Retrieved October 12, 2018, from http://www.isaaa.org/resources/publications/briefs/53/download/isaaa-brief-53-2017.pdf

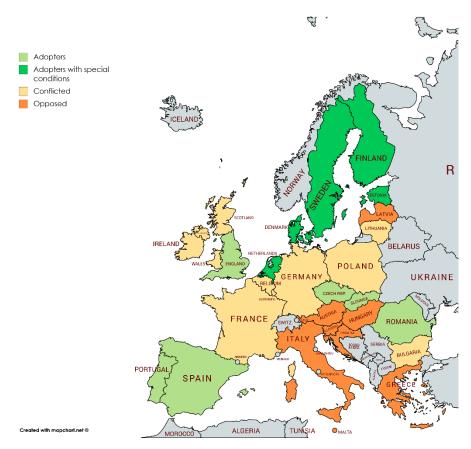


Figure 3.3.2 National differences within the EU depending on their acceptance of GM plants Source: Map is created based on data provided by Lucht (2015)



Analysing the regulatory framework between the two countries is a formidable task, since many actors are influencing the negotiating process and the development of the regulations.

Based on the information written and collected in Chapter II, the principles of GM plant risk assessment in the EU and US are slightly different in nature as summarised in **Table 3.2.3.1.** But the devil is always in the details. In general, the EU risk assessment procedures are conducted based on four principles: (1) molecular characterisation of the GM plant; (2) comparative analysis of compositional, phenotypic and agronomic properties; (3) safety assessment for humans and animals; and (4) safety assessment for the environment. While similar steps are applied in the US, the risk assessment for one product can be assessed by three different agencies with different roles, as summarized in **Table 2.3.1** and **Table 2.3.5**. Furthermore, unlike the EFSA, which only acts as a risk assessor without having the power to decide product authorisation, the US agencies at the same time are also playing an additional role as risk managers, which makes the process much easier and effective within their organisations.

The US regulatory framework for GM crops risk assessment may be regarded as less strict and more predictable when compared to the system in the EU. The FDA, through their voluntary notification program, may be seen as the best representative of the concept of the product-based approach enacted by the US governments. The GRAS provision for GMOs was added to prevent the FDA from having to evaluate every single component in the food supply, which made the process much more straightforward without disrespecting the safety aspect of human and animal health. The EPA regulates the pesticide residue and the PIP, while the USDA-APHIS regulates GM plants that may pose a risk to plant health. To conclude, each government has its own laws that reflect its own values. Although the US and the EU apply the same principles to the risk assessment process, their regulations and practices are significantly different.

Overall, this study supports the two recommendations from other scholars providing that the GM risk assessment process in the EU should be more evidence based, and that the EC should be urged to update their Communication about the precautionary principle to make the process more predictable.<sup>307</sup> Relying on criticism from inside the USDA-APHIS organisation,<sup>308,309</sup> and also from

<sup>&</sup>lt;sup>306</sup> EFSA. (2017). *Risk assessment of genetically modified plants*. Retrieved July 8, 2019 from <a href="https://www.efsa.europa.eu/en/discover/infographics/risk-assessment-genetically-modified-plants">https://www.efsa.europa.eu/en/discover/infographics/risk-assessment-genetically-modified-plants</a>

<sup>&</sup>lt;sup>307</sup> Lofstedt, R. (2014). The precautionary principle in the EU: Why a formal review is long overdue. *Risk Management*, 16(3), 137-163.

<sup>&</sup>lt;sup>308</sup> Marchant, G. E., & Stevens, Y. A. (2015). A new window of opportunity to reject process-based biotechnology regulation. *GM crops & food*, 6(4), 233-242

the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology, more effort should be put into the implementation of evidence based approaches and consistency in the laws with regards to the process of GM risk assessment. It is to be hoped that the EU will foster these new innovations.

 $<sup>^{309}</sup>$  McGinnis, E., Meyer, M., & Smith, A. (2012). Analysis of US genetically engineered crop regulation and litigation.  $\it Crop\ Science,\ 52(3),\ 991-1002.\ doi:10.2135/cropsci2011.08.0438$ 



#### **LEGAL TEXT**

- Commission Implementing Regulation (EU) No 503/2013 of 3 April 2013 on applications for the authorisation of genetically modified food and feed
- Directive 2001/18/EC on the deliberate release of GMOs into the environment
- Directive (EU) 2015/412 amending Directive 2001/18/EC as regards the power of the Member States to restrict or prohibit the cultivation of GMOs in their territory
- European Union for the European Union. 2012. Treaty on the Functioning of the European Union.
- Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
- Federal Food Drug and Cosmetic Act (FFDCA)
- Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents
- Regulation (EC) 1829/2003 on genetically modified food and feed
- Regulation (EC) 1830/2003 concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms
- Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority, and putting in place procedures in matters of food safety
- Plant Protection Act (PPA)

# CASE LAW

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Before the summer holiday in 2018, I was attending a thesis market and look for several possibilities of thesis topics as I want to do something related to food science and law. I also remember that in July, we were expecting the result of ECJ ruling on NPBTs and that has become my inspiration to choose this topic. I was excited when Kai Purnhagen agreed to supervise my thesis and that became the start of my journey. During the explanatory meeting, Kai gave me a lot of insight and ideas about the structure and content of my thesis. I would like to thank Kai Purnhagen for his help, feedback, and patience all this time. I am considered myself lucky to have another wonderful supervisor, Justus Wesseler. I would like to express my gratitude for his encouraging words and his idea to combine my thesis and internship to be able gaining a comprehensive knowledge about GMOs in the EU.

In addition, I would like to thank all families and friends who gave a full support to finish my thesis. Thank you my lovely husband—Romy (love you beb!), my best friend Lina who always accompanies me while working in Leeuwenborch till midnight, although she finished her thesis first :p, mom and dad for your support, my sisters: Mba Emmy, Mba Deny, and Ratih who prepared my wedding ceremony while I was busy with thesis. Also special thanks to Fred Celly for reviewing my thesis grammar and structure, Pai for becoming my lovely unofficial "study advisor", Piem who always encourages me with her wise words, and all my friends which I can't mention one by one.

I am fully aware that finishing this thesis is just a beginning, as this life is a never-ending learning process. One thing that I also learn during this journey is that in this life we can't always get whatever we want. However, if we keep doing our best and never give up, we may end up with something more than our expectation. One of my favourite quotes: "whoever does something persistently will succeed".

# APPENDIXES



# 1. List of FOIA received from EPA obtained through $\underline{\text{http://foiaonline.gov/}}$

Name of the dossier	Subject	Event	Crop	FOIA Releasing date
EPA-HQ-OPP-2014-0456-0008	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A.105 and Cry2Ab2 Proteins	MON 87751	Soybean	11/12/2018
Previously Released 524-528 vol 1-4	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry3Bb1 protein and genetic material (ZMIR13L)	MON 863	Corn	15/4/2019
Previously Released 524-575 vol 1-2	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A.105 and genetic material (ZMIR245)	MON 89304	Corn	15/4/2019
Previously Released 524-581 part 1-2	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cr3Bb1 and Cry34Ab1/Cry35Ab1	SmartStax	Corn	31/1/2019
Previously Released 524-576 vol 1-2	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A.105, Cry2Ab2, and genetic material (ZMIR245)	MON 89304 x MON 88017	Corn	31/1/2019
Previously Released 524-594	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1Ac and genetic material PV-GMIR9)	MON 87701	Soybean	15/4/2019

# 2. List of FOIA received directly from EPA

Name of the dossier	Year of Application	Subject and Event	Crop	FOIA Releasing date
Tracking Number:				
EPA-HQ-2019-003171				
releasable Application Docs for 69575- 2.pdf.pdf	1996	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A(c)	Corn	10/4/2019
releasable Application Docs for 524-619.pdf.pdf	2014	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A(c) and Cry2Ab2 proteins in MON 87751	Soybean	
releasable Application Docs for 264-	2008	Biopesticide registration for Bacillus Thuringiensis Cry1b	Cotton	

<u>1094.pdf.pdf</u>		protein for T304-40		
releasable Application Docs for 524- 478.pdf.pdf	1994	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A(c) protein	-	
releasable Application Docs for 62719- 696.pdf.pdf	2012	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1F protein for DAS-81419-2	Soybean	
Tracking Number:				
EPA-HQ-2019-003172				
releasable Application Package for 006615.pdf.pdf	2014	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A.105 and Cry2Ab2 protein in MON 87751	Soybean	12/4/2019
releasable Application Package for 006487.pdf.pdf	2000	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry2Ab protein	Corn	
releasable Application Package for 006512.pdf.pdf	2002	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1F protein	Cotton	
releasable Revised Application Package for 006600.pdf.pdf	2008	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry2Ae protein in GHB119	Cotton	
releasable Application package for 006484.pdf.pdf	2000	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry3Bb	Corn	
releasable Application Packet for 006490.pdf.pdf	2016	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A.105, Cry2Ab2, Cry3BB1, Cry1F, Cry34/45AB1 in Smartstax	Corn	
releasable Application package for 006515.pdf.pdf	2006	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1A.105 and Cry2Ab2 protein in MON 89304	Corn	
releasable Application package for 006528.pdf.pdf	2012	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1Ac and Cry1F proteins in DAS81419	Soybean	
releasable Application package for 006580.pdf.pdf	2014	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry3Bb1 protein in MON 87411	Soybean	
releasable Application package for 006481.pdf.pdf	2010	Biopesticide registration for <i>Bacillus Thuringiensis</i> Cry1Ab, Vip3Aa20, and Cry1F proteins in Bt11 x MIR162 x TC1507	Corn	

# 3. List of FOIA received directly from FDA

Name of the dossier	Event	Crop	Year of Application	FOIA Releasing date
BNF 26	Roundup Ready Gene, lines 1445 and 1698	Cotton	1995	26/2/2019
BNF 74	Insect-Protected Bollgard II Cotton Line 15985	Cotton	2000	7/2/2019
BNF147	MON 87403	Corn	2014	21/2/2019
BNF 148	MON 87419	Maize	2015	16/4/2019
BNF151	MZIR098	Corn	2015	14/12/2018
BNF157	MS11	Canola	2016	29/1/2019

# 4. List of Public Access Documents (PAD) received directly from EFSA

<b>Event/crop:</b> 305432x40-3-2 soybean	PAD acceptance date batch I: 6-3-2019
Name of the dossier	Subject
2008-02-19 EFSA Valid application _#47	Application for authorisation
2010-01-26_AI1 _#47	Response to questions on the restriction map of all inserted regions, specific band in the maize control
2013-12-04_AI2	Additional information in line with EFSA guideline: new bioinformatics data using an up-to-date databases, new information reported from new field trials
2014-02-25_AI3	Response to questions on the revision of PMEM to be in line with overall approach developed by the applicants and the EuropaBio
2014-06-19_AI5	Response to questions on the normal probability plot to identify outliers in the compositional analysis
2014-07-02_AI4_1	Response to questions on the additional experimental data to demonstrate the allergenicity of the whole soybean is comparable to the comparators
2014-07-22_AI6_#47	Response to questions on the methodology used and the results of new field trials, comparative analysis for the fatty acid profile of soybean phospholipids

2014-09-15_AI7_#47	Response to questions on the fatty acid profile of the unprocessed soybean
2014-10-03_AI8_#47	Response to questions on the appropriate statistical test, check for homosdasticity
2014-11-10_ AI9_#47	Response to questions on the agronomic, phenotypic, and compositional characteristics
2015-02-10_AI10_#47	Response to questions on the bioinformatics analyses using an up to date database
2015-04-14_VAI1_#47	Voluntary submission on up to date review of literature relevant to molecular characterisation, food/feed safety and environmental assessment
2015-04-14_VAI2_#47	Amended report on the endogenous allergen screen
2015-05-12 AI11_#47	Response to requests on the updated bioinformatics analyses on the complete nucleotide sequence of all inserts and their flanking regions on 3054223 soybean
2015-06-26_AI12_#47	Response to requests on analytical data on the fatty acid composition of the refined, bleached, and deodorised oil
2015-07-29_VAI3_#47	Voluntary submission on nutritional assessment information
2015-09-24_ AI14_#47	Response to requests on the additional experimental evidence (Southern and or PCR analysis)
2015-11-06 VAI4_#47	Voluntary submission on the comparative analysis of compositional and agronomic phenotypic characteristics
2016-01-29_AI15_#47	Response to requests on the complete set of compositional and agronomic phenotypic data from the 2011 field trials
2016-05-18_AI16_#47	Response to requests on quantitative support for the chosen model

Event/crop: Bt11 × MIR162 × MIR604 × GA21 maize PAD acceptance date batch II: 23-3-2019	
2012-06-14_Valid application AP86	Part I - Technical dossier, Part II – Summary, Part III - Cartagena Protocol, Part IV – Labelling, Part V - Detection method, Part VI - Additional information, References
2013-04-23_Additional info protein interaction & agronomy	Response to requests on potential interaction on the newly expressed proteins, NTO, and agronomic assessment on stacked hybrid and herbicide regimes applied
2014-06-13_Additional info bioinfo (crs 3)	Response to requests on updated bioinformatics analyses
2014-06-19_Additional info Vit A (crs 4)	Response to requests on beta carotene level of the compositional study
2014-07-24_Additional info bioinfo_ORF (crs 3)	Response to requests on update bioinformatics analyses of the newly expressed proteins, allergenic or toxic proteins, and region flanking the inserts

Assessment of sequence similarity of the Cry1F proteins to known allergen and toxins
Literature search between 2012-2014
Complemented for expressions and composition data
Response to requests on repeating bioinformatics analyses and perform supplementary comparative compositional analyses
Bioinformatics analyses for assessing potential allergenicity of newly expressed proteins
Resubmit raw data less than 100MB
MIR162 Bioinformatics raw data
GA21 sequence information
Sequence similarity assessment and bioinformatics analyses of the putative reading frames
Response to requests on the likelihood of ORFs expressions, as well as an update of the Cartagena Protocols and Labeling Proposal and PMEM plans
Review of the literature related to the events
Response to requests on the bioinformatics analyses
Response to questions on composition of carotenoid
Response to requests on the bioinformatics analyses of putative allergens and toxins
Sequencing on the several events
Response to questions on saponification and the relevant hits
Response to questions on the literature search