

Literature Synthesis Report

Gene Technology in Agriculture

CONTENT

Foreword.....	04
Molecular and Metabolic Effects.....	05
Health Effects.....	07
Ecological and Agronomic Effects.....	09
Current Legal Framework.....	11
Workflow.....	13

ABOUT

Address

Reatch! Research. Think. Change.
Binzstrasse 12 | 8045 Zürich

Contact

info@reatch.ch

Website

www.reatch.ch

Texts

Sandro Christensen (Health Effects)
Hélène Gonnet (Ecological and Agricultural Effects)
Servan Grüninger (Coordination)
Michael Kümin (Molecular Effects)
Ueli Merz (Support Ecological and Agricultural Effects)
Dario Piccchi (Current Legal Framework)

Image

Nora Gamper

Foreword



An Insightful Process

It is with great pleasure that I present to you the Literature Synthesis Report that my colleagues wrote on behalf of the Swiss Academy of Sciences (SCNAT). This document contains the executive summary of the four chapters of the Literature Synthesis Report:

1. Executive summary of the chapter “Molecular and Metabolic Effects” by Michael Kümín (133 publications)
2. Executive summary of the chapter “Health Effects” by Sandro Christensen (82 publications)
3. Executive summary of the chapter “Ecological and Agronomic Effects” by Hélène Gonnet (189 publications)
4. Executive summary of the chapter “Current Legal Framework” by Dario Picocchi

Each chapter gives an overview of the most important findings regarding the three key questions defined by the SCNAT Evidence Review Group (ERG) and over the current legal framework regarding GMOs and, specifically, GM crops in Switzerland and Europe. Details on the key questions as well as on the workflow are outlined in the fifth chapter of this report (“Workflow”).

This summary marks the conclusion of a challenging but insightful process that lasted almost four years and that was accompanied by intense scientific discussions. Therefore, the Literature Synthesis Report underwent multiple rounds of revisions including various comments and remarks from the members of the ERG for which we are very grateful. In order to keep the workflow as transparent as possible, the chapter “Workflow” also contains details on the review process.

I hope that the information summarised herein will provide a solid basis for future societal and political discussions on genetically modified organisms in the context of agriculture and agricultural products.

Servan Grüniger

President Reatch! Research. Think. Change.

Executive Summary

Modern plant breeding is nowadays routinely used to change various traits of agricultural products. This can be done using a wide range of breeding techniques some of which are labelled as conventional and some of which are grouped under the umbrella term of “genetic engineering”. As such, the chapter “Molecular and Metabolic Effects” of the Literature Synthesis Report aims to outline the effects of classic and novel genetic engineering techniques on a plant’s genome and its molecular and metabolic composition in comparison with the effects that conventional breeding methods have.

However, it is important to stress that this distinction is mainly based on historical path-dependencies rather than theoretically or empirically consistent criteria. In short, all those breeding techniques that were already in use at the onset of the biotechnological revolution in the 1970s are commonly regarded as conventional breeding techniques in Switzerland and Europe whereas newer breeding methods fall into the category of genetic engineering.

Due to the diversity of techniques and plant species that are routinely assessed in scientific publications and regulatory reports, generalising statements should be met with some caution. Nevertheless, we would like to point out some conclusions based on the detailed assessments provided in the full chapter (linked to below):

- All plant breeding techniques modify the genetic structure and the molecular composition of a plant to some extent, regardless of whether they are deemed “conventional breeding techniques” or “genetic engineering techniques”.
- There is no plant breeding technique for which one can make the claim that its use will lead to no unintended effects whatsoever or - to the contrary - that its use will always lead to unintended effects.
- Different breeding techniques (conventional and genetic engineering) are often used in combination with each other in the process of the creation of a novel plant variety so that the molecular and metabolic changes of these techniques are not always straightforward to disentangle.
- Even within the same methodological framework, different applications can have different effects on the genetic structure and the molecular composition of the resulting plants.
- The application of new genetic engineering techniques progresses at a rapid pace within and outside the field of plant breeding and therefore warrants a continuous scientific assessment of its effects on the molecular and metabolic composition of plants.

These findings might appear trivial at first but they are important to keep in mind with regard to risk assessments and policy decisions as debates about GMO safety often confound the safety of a particular crop with the safety of the breeding technique that led to the development of said crop. Also, as the state of knowledge about a particular genetic engineering technique rises over time, its effects on the molecular structure and the metabolic composition of the modified plants can be analysed more precisely which might warrant a re-assessment of safety regulations if new evidence arises.

Detailed Results

The detailed results of this chapter can be found under the following link:

<https://docs.google.com/document/d/13hK2jCVZ2hZkOqSv9boAILzsG1ZJXuQFrMS-bhjU7FE/edit?usp=sharing>

Please note that this is intended to be a living document, that is, it is open for comments and updates. Please follow the following rules when doing so:

- State precisely what should be updated.
- Explain why the update adds something new to the Literature Synthesis Report or in which regard a correction is necessary.
- Refer to a peer-reviewed publication according to the inclusion criteria outlined in the “Workflow” chapter to back up your comment.

The comments will be screened at least once a year. Implementation of the comments and suggestions hinges on the available resources of the authors and editors. If you want to get involved as an editor, contact info@reatch.ch.

The version on which the executive summary in this document is based and which serves as the conclusion of the literature synthesis process accompanied and supervised by the SCNAT ERG is labelled as “Literature Synthesis Report, Gene Technology in Agriculture, 2021.04.05, SCNAT ERG”. It should be noted that all potential future updates and corrections to the online documents are not part of the process outlined in the chapter “Workflow” and thus are not part of this Literature Synthesis Report as commissioned by the SCNAT.

Executive Summary

In this chapter, we tried to give an explanatory and broad perspective on the study findings of positive and negative health effects of GM crops. In general, the literature provided by the Evidence Review Group reports no additional risk of adverse health effects of GM crops when compared to conventional crops. It is important to stress, however, that this statement only holds for the particular GM and conventional crops that were available on the market at the time of publication. In other words: It is a statement about particular products not about the breeding technologies in general that gave rise to these products. Conventional breeding and genetic engineering can both lead to potential health hazards when improperly deployed.

In addition, the literature assessment has unearthed unanswered questions about transparency, appropriate study designs to tackle specific health related questions and proper statistical analysis. Potential health hazards arising from the consumption of food are notoriously difficult to analyse rigorously due to many known confounders that are involved and whose effects are difficult to disentangle. Hence, with the potential exception of acute strong toxicity, the health effects of consumption of both conventionally bred and genetically engineered crops can hardly ever be assessed in a conclusive way.

Scientists are well aware that absolute safety is not achievable despite governmental regulation. For that reason, different reports stressed the importance of post market monitoring to identify any long-term health effects from GM crops. This is in line with the EFSA's guideline for risk assessment which recommends post market monitoring for food and feed derived from GM plants. However, it should be mentioned that health hazards can arise irrespective of the breeding technique employed to produce a particular crop and thus the assessment of such hazards should focus on the particular product in question.

Detailed Results

The detailed results of this chapter can be found under the following link:

<https://docs.google.com/document/d/1-dpIOzgskCtkoxGm-eZEhAjqRgxBNsJanGEYVFrNCEI/edit?usp=sharing>

Please note that this is intended to be a living document, that is, it is open for comments and updates. Please follow the following rules when doing so:

- State precisely what should be updated.
- Explain why the update adds something new to the Literature Synthesis Report or in which regard a correction is necessary.
- Refer to a peer-reviewed publication according to the inclusion criteria outlined in the "Workflow" chapter to back up your comment.

The comments will be screened at least once a year. Implementation of the comments and suggestions hinges on the available resources of the authors and editors. If you want to get involved as an editor, contact info@reatch.ch.

The version on which the executive summary in this document is based and which serves as the conclusion of the literature synthesis process accompanied and supervised by the SCNAT ERG is labelled as “Literature Synthesis Report, Gene Technology in Agriculture, 2021.04.05, SCNAT ERG”. It should be noted that all potential future updates and corrections to the online documents are not part of the process outlined in the chapter “Workflow” and thus are not part of this Literature Synthesis Report as commissioned by the SCNAT.

Executive Summary

With regard to the ecological and agronomic effects, the following findings should be highlighted:

- Both the ecological and the agronomic effects of the GM crops currently applied in agriculture do not solely depend on the crop itself but also on the ecological and agronomic environment in which they are applied. That is, the same crop can have different effects on the key ecological and agronomic factors such as yield, pest control or biodiversity.
- Most currently grown GM crops are applied in heavily industrialised agricultural settings in which they can yield GM crops both agronomic and ecological improvements. However, these findings cannot be extrapolated to other agricultural settings without additional research.
- Over-reliance on herbicide-resistant crops in combination with excessive use of herbicides has led to the emergence of herbicide-resistant weeds in many agricultural settings.
- When it comes to the Swiss context, there is a scarcity of translatable findings that fit the Swiss agricultural setting. Potential agronomic or ecological benefits of GM crops need to be assessed on a case-by-case basis.

It should be stressed that both the problems as well as the benefits of GM crops that arise in a particular ecological and environmental setting are linked to the specific trait of said crops and not the way in which these traits were introduced into the plants. In other words, problems such as the emergence of herbicide resistance or the reduction of biodiversity can arise with or without GM crops. Similarly, benefits such as yield gains or reduction of pesticide usage can be achieved with conventionally bred and genetically engineered crops. The relative advantages and disadvantages of the different crops are thus not a function of the breeding technique used to create the crop but of the specific trait introduced in combination with the ecological and agronomic environment it is used in.

As with the results in the previous chapters, these findings might be perceived to be trivial. However, it is again important to highlight the crucial distinction between an assessment of the ecological and agronomic effects of a particular breeding technique and an assessment of the effects of a particular crop itself. Whereas there is evidence for both problems and benefits arising from particular GM crops in certain contexts, the assessment of the literature provided by the ERG did not provide any evidence that genetic engineering as a breeding technique poses a larger ecological threat than conventional breeding.

Finally, it should be mentioned that due to the complexity of ecological and agronomic systems it can be difficult to disentangle the effects of a particular crop from other potentially confounding factors. This holds for both aggregated observational data and detailed experimental data from the laboratory. Whereas the interpretation of observational data is prone to ecological fallacies, laboratory data is often hampered by limited external validity. Hence, thoroughly planned and conducted field experiments that are representative of the Swiss agricultural context promise to provide the most valid insights into the ecological and agronomic effects of GM crops.

Detailed Results

The detailed results of this chapter can be found under the following link:

https://docs.google.com/document/d/15D_ybRRSka9EvTaM_M_-Nx0DzeuhlI9uVYHDg8NWHkQ/edit?usp=sharing

Please note that this is intended to be a living document, that is, it is open for comments and updates. Please follow the following rules when doing so:

- State precisely what should be updated.
- Explain why the update adds something new to the Literature Synthesis Report or in which regard a correction is necessary.
- Refer to a peer-reviewed publication according to the inclusion criteria outlined in the “Workflow” chapter to back up your comment.

The comments will be screened at least once a year. Implementation of the comments and suggestions hinges on the available resources of the authors and editors. If you want to get involved as an editor, contact info@reatch.ch.

The version on which the executive summary in this document is based and which serves as the conclusion of the literature synthesis process accompanied and supervised by the SCNAT ERG is labelled as “Literature Synthesis Report, Gene Technology in Agriculture, 2021.04.05, SCNAT ERG. It should be noted that all potential future updates and corrections to the online documents are not part of the process outlined in the chapter “Workflow” and thus are not part of this Literature Synthesis Report as commissioned by the SCNAT.

Executive Summary

Even though the legal framework revolving around GMOs was not within the main scope of this review, we found it important to provide the SCNAT Evidence Review Group with an overview over the legal situation regarding safety testing and approval procedure of genetically modified foodstuffs in Switzerland. However, we do not make any recommendation with regard to future adaptation of or changes to these frameworks since we believe this should be discussed in a subsequent policy dialogue.

Main question

How are unintended effects addressed before a new crop variety reaches the market (testing procedures and approval requirements for non-GM and GM crops)?

Specific questions

- Which regulations are relevant for the licensing procedure for foodstuffs containing GMOs?
- How are GMOs legally defined and which breeding methods fall under this definition?
- What obligations must be observed when dealing with foodstuffs containing GMOs?
- What are the legal licensing requirements for GMO-products in general?
- Are there any additional licensing requirements for foodstuffs containing GMOs?

Legal Framework

In Switzerland, the general statutes that are decisive for questions concerning foodstuffs containing GMOs are the Gene Technology Act (GTA) and the Foodstuffs Act (FSA). Most of the details regarding the licensing procedure for foodstuffs containing GMOs are regulated in the corresponding ordinances (RO, LGV, VGV, LIV).

Legal Definition of GMOs

Pursuant to art. 5 para. 2 GTA, GMOs are all organisms «in which the genetic material has been altered in a way that does not occur under natural conditions by crossing or natural recombination». Each organism resulting from (new) genetic engineering methods has to be examined individually to determine whether or not the altered organism can be classified as a GMO.

Licensing Procedure for GMO-Containing Foodstuffs

The marketing of foodstuffs containing GMOs is subject to federal licensing. Any foodstuffs containing GMOs must not only fulfill the general marketing licensing requirements according to the RO but also the specific food law (licensing) requirements.

The data and information to be submitted to the competent authorities are described in detail in the annexes to the statutes; with direct references to European directives. To assess the licensing application, the competent authority relies on the data submitted by the applicant. The authorities do not commission their own examinations.

Detailed Assessment

The detailed results of this chapter can be found under the following link:

<https://drive.google.com/file/d/1eZQzbusHhMF9SbSx4tl8jpVWQ34dXECV/view?usp=sharing>

Workflow

Background

It was an ambitious goal: The Swiss Academy of Sciences wanted to bring together scientists and stakeholders with very different perspectives on genetic engineering in agriculture in order to summarise the currently available scientific evidence with regard to three levels:

1. What are the effects on the genome and the molecular and metabolic composition within genetically modified crops compared to conventionally bred crops?
2. What are the health effects on humans and animals of genetically modified crops compared to conventionally bred crops?
3. What are the ecological and agronomic effects of genetically modified crops compared to conventionally bred crops with a special focus on the Swiss context?

In addition, the current legal regulations of genetically modified crops were to be assessed in the context of the Swiss law. The goal of this endeavor was to provide an evidential basis for policy-makers to base their regulations on.

It should be stressed that after the meeting of the ERG on the 29th of August 2018, several changes to the assessment criteria of the literature and the inclusion policy were requested by the members of the ERG. The following sub-chapters serve to explain the process. In addition, the whole screening and writing process was conducted using Google Documents, allowing for complete traceability of changes made to the core documents of this review.

Key Questions

The key questions as well as the inclusion criteria for this review were defined by the members of the SCNAT Evidence Review Group (ERG). In short, we were asked to address the following three key aspects:

- Molecular and metabolic effects: What are the effects of classic (transgenesis) and new genetic engineering technologies (e.g. cisgenesis, genome editing) on a plant's genome and its molecular and metabolic composition? How do these effects compare to those observed when using conventional breeding technologies including mutagenesis?
- Health effects: What positive and negative effects on human and animal health have been observed from the consumption of GM crops in comparison with conventional crops?
- Ecological and agronomic effects: What positive and negative agronomic and environmental effects have been observed for GM crops in field trials and agricultural systems relevant to the Swiss context? What do scientific models predict?

For key aspect 1 ("Molecular and metabolic effects"), there were no specific crops that were excluded from the analysis. Rather the analysis focuses on the effects of different breeding techniques on the plants' genome and metabolome in general. For key aspect 2 ("Health effects"), all commercialised crops used as food or feed for which scientific evidence exists are considered. For key aspects 3 ("Agronomic & ecological effects"), the Literature Synthesis Report focused on commercialised crops and on non-commercialised crops that are close to the market and for which sufficient scientific evidence existed. The review only included crops that might be relevant for the Swiss market.

For studies on commercialised crops, the following questions and criteria were kept in mind:

- Are the results of the studies applicable to the Swiss context? Are there studies from countries that use GMO with similar agricultural systems as Switzerland?
- Where scientific literature exists, key aspects were analysed with regard to the following four agricultural settings
 - conventional farming without GMO
 - conventional farming with GMO
 - organic farming without GMO
 - “organic” farming with GMO (i.e. farming that follows the same practices as organic agriculture but uses GMO)

For close-to-market crops, the following questions had to be addressed:

- Are there valid scientific studies on ecological and agronomic effects?
- If yes, which questions do they address and which are left unaddressed?
- If simulation and model studies are done:
 - Do the assumptions hold up? Have similar studies been done for other countries and have the assumptions held up there?
 - Are the assumptions applicable to the Swiss context?
- Where scientific literature exists, also analyse the non-commercialised crops in the following four context:
 - conventional farming without GMO
 - conventional farming with GMO
 - organic farming without GMO
 - “organic” farming with GMO

More details on the key questions as defined by the ERG can be found here:

<https://docs.google.com/document/d/1rD1l6nUdUuHfCe8zSJq11dUze3UWi0TEpjdUwTI44Q/edit?usp=sharing>

Literature Collection

The literature to be considered for this report was provided exclusively by the members of the SCNAT Evidence Review Group (ERG), hence it is important to stress that this report is not a systematic review of the available literature because only publications submitted by ERG members were assessed. However, the literature submitted by the ERG did not cover all relevant questions equally so that there was an abundance of literature with regard to some topics whereas other issues were hardly covered by any of the articles that were submitted.

In order to collect the literature submitted by the evidence review group, we adopted a multi-tiered approach. First, we screened the literature provided to us at the very onset of the evidence review process for any reviews, reports and meta-analyses that might encompass a large part of the submitted literature and assigned them to “Literature List A” (105 publications), the remaining literature was assigned to “Literature List B” (192 publications). In addition, we assigned one of the referenced publications (“Ferment et al. 2017”) its own literature list, namely “Literature List C” (737 publications). This was necessary because the publication in question was not a review article or report per se, but rather a list of individual articles for which the authors claimed a relation to the topic of genetically modified crops. Hence, we decided to screen those articles individually.

All the literature lists can be found here:

https://docs.google.com/spreadsheets/d/19ug_nvHEmiQxFGkH7HF-0w6EHjV9v8onhqp3oXQPWfo/edit?usp=sharing.

In a second step, we asked the members of the ERG to provide us with any reviews which were not yet represented on the list of collected reviews ("Literature List A") *OR* covered by them *AND* which are relevant for the key questions *AND* which fulfill the inclusion criteria. In addition, we asked for any research articles (e.g. experimental studies) which were not covered by the reviews listed in Literature List A *AND* which are relevant for the key questions *AND* which fulfill the inclusion criteria. We then assembled all the publications sent to us in "Literature List D" (251 publications). In total, we had to screen 1285 individual publications. From this point onwards, the literature review was performed blinded, i.e. without knowing which member of the ERG provided us with which set of articles. This was done in order to prevent a conscious or unconscious bias in assessing the articles.

Screening and Annotating Literature

After having received the literature from the members of the ERG, we screened the publications in each list in a multi-tiered manner. First (I), we checked whether a publication was already covered by one of the reviews, meta-analyses or reports assembled in Literature List A. If the publication was already cited by any of the papers in Literature List A, we excluded it. We made sure to reduce the number of false positives to zero, but allowed for a potentially large number of false negatives. In this context, a false positive describes the case where we would incorrectly claim that a publication was already covered by one of the papers in Literature List A, while a false negative describes the situation in which we incorrectly failed to exclude a publication that was already cited. In other words: we made sure that we did not miss any publication that was not yet cited, but there is the possibility that we included some publications, which were already cited by one or more of the reviews. This is due to the inaccuracies of the semi-automated extraction method adopted to retrieve the references of the publications on Literature List A.

We then checked whether the remaining publications were within the scope of the evidence review and removed all those that were not. Finally, we checked whether the remaining publications had any severe methodological limitations, were retracted or simply not peer reviewed and removed them from the analysis. In addition, we had to remove additional publications because they were inaccessible, mainly because they were written in a language which none of the authors of this review were able to understand. Table 1 gives an overview over the screening process and the number of publications removed at each step.

It is important to mention that removing a paper from the analysis of this literature review is in most cases no judgement about the quality of the scientific findings described in this paper. If we removed a paper because it was already covered by a publication on Literature List A or because it was beyond scope, we stopped the evaluation at this point. Hence, we did not additionally assess the quality of the publication removed. Examples for papers which were removed can be found further below.

List	Initial number of publications	I Covered by a publication in List A	II Beyond scope	III Not peer reviewed / retracted / severe limitations	IV Not accessible	Included as of August 29th 2018
A	105	-6	-19	0	-1	79
B	192	-85	-60	-15	0	32
C	737	-281	-338	-13	-9	96
D	251	-72	-85	-7	-1	86
Total	1285	-444	-502	-35	-11	293

Table 1: Overview over multi-tiered pre-analysis screening including the number of publications removed at each step in each publication list. After the screening, almost 300 publications were included in the evidence review by the 29th of August 2018. The discrepancy to the final number of publications included arises due to multiple review rounds in which additional publications were requested to be included on various grounds by the members of the ERG (see below).

Categorising and Analysing the Literature

After the conclusion of the pre-screening phase, we defined categorisation factors for further classification of the remaining publications. Note that some of these factors might be redundant in the sense that one factor contains all the information present in another factor. This redundancy was intentional in order to increase the robustness of the classification against unintentional labelling mistakes.

The Evidence Review Database contains all labelled and categorised publications that were included into the evidence review by the 29th of August 2018 as well as all the publications that were included upon request by the members of the ERG after that. It can be found here:

https://docs.google.com/spreadsheets/d/1AkjJcf74bPVFMH3uEfsQ2nyi8YeYVXH_QBQsATqU2yE/edit?usp=sharing

Type of Publication

We distinguished between:

- *Individual Study/Article*: Any publication describing original research findings
- *Systematic Review*: A systematic and structured approach to review all the relevant literature on a topic. The methodology of the review as well as the inclusion and exclusion criteria must be described
- *Meta-Analysis*: Any systematic review that uses statistical methods to combine the numerical results from the analysed studies.
- *Non-systematic Review*: Any review without indication of a clear methodology and/or inclusion criteria
- *Report*: Any publication that summarised and reported the body of evidence of a specific project or set of projects. Reports are usually mandated by national or international agencies to tackle a specific question.
- *Discussion/Editorial*: Any text discussing or reflecting on the existing body of evidence with regard to a specific question but without being as exhaustive as a review
- *Correspondence/Comments*: Any commentary or correspondence letter revolving around GM crops published in peer-reviewed journals

Information about Conflict of Interest and Funding Sources

In addition, we assessed the following factors regarding potential conflicts of interests and the funding source:

- *Paragraph/Statement about conflict of interests (1 = yes / 0 = no)*: We set this factor to 1 if the publication contained any paragraph or statement addressing potential conflicts of interests.
- *Conflict of interest declared (1 = yes / 0 = no / NA = information missing)*: We set this factor to 1, if the authors declared a conflict of interest. We set it to 0, if the authors declared that they do not have any conflict of interest. If there was no statement or paragraph about potential conflicts of interest, we set the factor to NA.
- *Information about Funding Source (1 = yes / 0 = no)*: If the publication provided any information about the funding source of the research described, we set the factor to 1.
- *Funding source (NA = information missing)*: If the publication provided information about the funding source of the research described, we explicitly stated the funding source(s) in this column. Otherwise, we set the corresponding cell to NA.

Note that the factor “conflict of interest declared” only indicates whether the authors themselves openly declared a potential conflict of interest. It does not cover all those cases in which a conflict was present, but not declared. However, these cases often become apparent when looking at the funding source. In these cases, we often left a comment highlighting the possibility of a conflict of interest in the sense of any economic, institutional or political ties that might influence the objectivity of the research conducted. Examples for publications for which no conflict of interest was declared, but where a conflict of interest was obviously present:

- Sanders, R. A., and William Hiatt (2005), “Tomato transgene structure and silencing” (authors are employed by an agricultural company selling GMOs)
- Price, B., and Cotter, J. (2014), “The GM Contamination Register: a review of recorded contamination incidents associated with genetically modified organisms (GMOs),” 13. (authors are working for NGOs opposing GMOs)
- Comas et al. (2014), “No effects of *Bacillus thuringiensis* maize on nontarget organisms in the field in southern Europe: a meta-analysis of 26 arthropod taxa” (partially funded by seed companies)

On the other hand, we assumed that funding from a governmental agency, a governmental funder or public or private university was not a conflict of interest. In these cases, we did not leave any comment regarding potential conflicts of interest.

Information about Methodology

Finally, we assessed whether the publications mentioned any kind of methodology and if yes, very briefly summarised it:

- *Methodology mentioned (1 = yes / 0 = no)*: We set the factor to 1 if the methodology was mentioned within the publication and we set it to 0 if not.
- *Methodology (NA = information missing)*: Quick summary of the methodology used

Additional Factors and Categories Dependent on Topics

For each of the three key topics, we defined additional categorisation factors based on the key questions defined by the ERG. These factors and their description can be found in the detailed assessments of each chapter.

Discussion of Reasons for Excluding Papers (incl. Examples)

Exclusion of Pesticide Effects without Relation to GMOs

Several members of the ERG pointed out the importance of addressing potential interactions between herbicide-resistant crops and the corresponding herbicides administered. We agreed to this. Hence, we included all publications which looked at the molecular and metabolic effects, at the health effects, and at the ecological and agronomic effects of herbicides used in conjunction with herbicide-resistant crops.

However, we excluded all those publications which assessed these effects without any relation to GM crops. Even though the thorough assessment of pesticide effects on our health and our environment is of utmost societal importance, it is not part of this evidence review as outlined by the key questions defined by the ERG.

Exclusion of Crops not Grown in Switzerland and Ecosystems Clearly Different from Switzerland

As outlined in the document containing the key questions, this evidence review was conducted with a specific focus on Switzerland. Hence, we excluded all publications and findings revolving around crops that are not grown in Switzerland (such as cotton) or revolving around ecosystem effects that are not comparable to Swiss ecosystems (such as publications focusing on ecological effects in tropical countries). Again, this is no judgement about the merit of assessing these questions, it simply stems from a strict reading of the inclusion criteria.

Exclusion of Studies Focusing on Molecular Effects in Animal Cells

We also excluded all publications which exclusively focused on the molecular effects of genetic modification in animal cells. Even though the shared evolutionary history of plants and animals allows for generalisation of findings up to a certain degree, it is not prudent to transfer findings from animal cell cultures to plants without any additional corroboration using data from plants. In addition, there has been ample evidence that the effect of one and the same genetic engineering technique can be radically different across biological kingdoms.

Exclusion of Studies Focusing on Ethical and Political Questions

Finally, we excluded all publications focusing on policy recommendations or ethical considerations. The focus of this review lies on the assembly of the available scientific evidence regarding GM crops. Ethical and political considerations can be used to guide the discussion about these findings, but are not part of the scientific findings themselves. However, we provide the ERG with an overview over the current legal framework regarding GM crops in Switzerland and Europe (see Chapter 4).

Examples of Papers that Were Excluded

Examples of publications that were deemed to be beyond scope

- *Policy questions:* Jordan et al. (2017), "A cooperative governance network for crop genome editing: the success of governance networks in other areas could help to find common ground for applying genome editing in agriculture."
- *Pesticide effects without connection to GM crops:* Colborn, T. (2006), "A case for revisiting the safety of pesticides: a closer look at neurodevelopment"
- *Focus on a crop which is not grown in Switzerland:* Donegan et al. (1995), "Changes in levels, species and DNA fingerprints of soil microorganisms associated with cotton expressing the *Bacillus thuringiensis* var. *kurstaki* endotoxin."
- *Molecular effects in animal cells:* Elbashir et al. (2001), "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells"

Examples of publications which were not accessible

- *Language barriers*: Sun et al. (2003), "Effect of transgenic Bt rice planting on soil enzyme activities". (Article in Chinese)
- *Paywall*: Malatesta (2009), "Animal feeding trials for assessing GMO safety: answers and questions" (article is behind a paywall, also unavailable from "scihub" and "b-ok.org"; buying a day pass and requesting the publication via "researchgate" did not yield access either)

Examples for publications which were not peer reviewed

- *Predatory Journal*: Abdo et al. (2014), "Feeding Study with Bt Corn (MON810: Ajeeb YG) on Rats: Biochemical Analysis and Liver Histopathology" (published in a predatory journal: SCIRP - Scientific Research Publishing; <https://beallist.weebly.com/>)
- *News article*: Kloor, K. (2015), "Agricultural researchers rattled by demands for documents from group opposed to GM foods."

Examples for publications which were retracted and/or fraudulent

- *Retracted*: Mezzomo et al. (2013), "Hematotoxicity of Bacillus thuringiensis as spore-crystal strains Cry1Aa, Cry1Ab, Cry1Ac or Cry2Aa in swiss albino mice."
- *Fraudulent*: Tudisco et al. (2015), Genetically modified soybean in a goat diet: Influence on kid performance (see: http://napoli.repubblica.it/cronaca/2016/02/09/news/universita_-133079638/)

Examples for publications that had severe methodological shortcomings

- *Methodological & statistical shortcomings*: Cirnatu et al. (2011), "Multiple organ histopathological changes in broiler chickens fed on genetically modified organisms." (e.g. the publication fails to fully disclose the results and the statistical analysis; the statistical tests that were performed were not mentioned; the authors fail to fully disclose the total number of events in each treatment group; pictures are presented without showing any control pictures)

First review round: Discussion of the Process after the Meeting of the ERG on the 29th of August 2018

On the 29th of August 2018, the members of the SCNAT Evidence Review Group met to discuss the preliminary findings of the Reatch Literature Synthesis Report. The e-mail correspondence as well as the meeting minutes can be found here:

<https://drive.google.com/drive/folders/1N4ZYgQGagJ1tc624BbuRI8T0DAYiDaUz?usp=sharing>

The inputs and feedback from the ERG were incorporated in the way described here:

<https://docs.google.com/document/d/1-weUlw7k0LQIEh-iXeWdc77gt80-biiQX8cHUkKZrs>

Second review round: Discussion of the Process after the 18th of April 2019

On the 18th of April 2019, the members of SCNAT ERG received the revised version of the Literature Synthesis Report with the request for feedback by the 3rd of May (the deadline was eventually extended by a month). Even though it was clearly communicated that at this stage no additional literature suggestions should be made, several reviewers did so anyway and it was the explicit request of the SCNAT to assess each suggestion individually. The corresponding e-mail correspondence as well as the point-by-point responses to the statements made by ERG members can be found here:

https://drive.google.com/drive/folders/1GpV9fXWuQK50RXXQu7QdHjYHyYGa_e-X?usp=sharing

Third review round: Discussion of the Process after the 23th of March 2020

On the 18th of April 2019, the members of SCNAT ERG received the revised version of the Evidence Report with the request for feedback by the 3rd of May (the deadline was eventually extended by a month). Even though it was clearly communicated that at this stage no additional literature suggestions

should be made, several reviewers did so anyway and it was the explicit request of the SCNAT to assess each suggestion individually. The corresponding e-mail correspondence as well as the point-by-point responses to the statements made by ERG members can be found here:

https://drive.google.com/drive/folders/1ij0z1dKCA3_b2UHwpueTzDM_v3goosYo?usp=sharing

Number of Publications included as of the 05th of April 2021

- | | |
|---|------------------|
| • “Molecular and Metabolic Effects”: | 133 publications |
| • “Health Effects” by Sandro Christensen: | 82 publications |
| • “Ecological and Agronomic Effects”: | 189 publications |