BGF biotech-gm-food

Selected and edited by **BGF** Jany

Literatursammlung zum EuGH-Urteil (C-528/16), zur genrechtlichen Einordnung von Mutagenese Verfahren und zu Anwendungen der neuen Züchtungsverfahren

Stand: Juni 2021

Urteile:

Das **EuGH-Urteil** zur rechtlichen Einordnung von Mutagenese Verfahren:

Urteil des Gerichtshofes (Große Kammer) vom 25. Juli 2018 in der Rechtsache C-528/16 betreffend ein Vorabentscheidungsersuchen nach Art, 267 AEUV, eingereicht vom Conseil d´Etat (Staatsrat, Frankreich mit Entscheidung vom 3.Oktober, beim Gerichtshof eingegangen am 17.Oktober 2016 in dem Verfahren Confédération paysanne, Réseau Semences Paysannes, Les Amis de la Terre France, Collectif VigilanceOGM et Pesticides16, Vigilance OG2M, CSFV49, O GM dangers, Vigilance OGM 33, Fédération Nature et Progrès gegen Premierministre, Ministère de l'Agriculture, de'Agroalimentaire et de la Forêt

"Durch Mutagenese gewonnene Organismen sind genetisch veränderte Organismen (GVO) und unterliegen grundsätzlich den in der GVO-Richtlinie vorgesehenen Verpflichtungen"
"Von diesen Verpflichtungen ausgenommen sind aber die mit Mutagenese-Verfahren, die herkömmlich bei einer Reihe von Anwendungen verwendet wurden und seit langem als sicher gelten, gewonnenen Organismen, wobei es den Mitgliedstaaten freisteht, diese Organismen unter Beachtung des Unionsrechts den in der GVO-Richtlinie vorgesehenen oder anderen Verpflichtungen zu unterwerfen."
https://eur-lex.europa.eu/legal-content/DE/TXT/PDF/?uri=CELEX:62016CJ0528&from=DE

hierzu auch:
https://www.biotech-gm-food.com/kommentare/eugh-urteil-mutagenese-ist-gentech

GA Bobek – EuGH: **Vorabentscheidung von Generalanwalt Bobek zur Mutagenese und Gentechnik**
Pressemeldung: German:
http://bit.ly/2Dlgsav
English:https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-01/cp180004en.pdf
Vollständiger Text: deutsch: http://curia.europa.eu/juris/document/document.jsf?text=&docid=198532&pageIndex=0&doclang=DE&mode=req&dir=&occ=first&part=1&cid=779174#Footref12
English: http://curia.europa.eu/juris/document/document.jsf?text=&docid=198532&pageIndex=0&doclang=EN&mode=req&dir=&occ=first&part=1&cid=779292

Hierzu auch: **Genome Editing ist nicht immer Gentechnik und führt nicht immer zu GVOs**
https://www.biotech-gm-food.com/aktuelles/mutagenese-nicht-immer-gentechnik

Staatsrat: Umsetzung des EuGH-Urteils

Conseil d'État, 7 février 2020, Organismes obtenus par mutagenès
https://www.conseil-etat.fr/ressources/decisions-contentieuses/dernieres-decisions-importantes/conseil-d-etat-7-fevrier-2020-organismes-obtenus-par-mutagenese

Conseil d'État: **The Council of State (Conseil d`État) has implemented the CJEU ruling on mutagenesis procedures.** According to the judgement, organisms obtained by new procedures for genetic modification (genome editing) are genetically modified organisms (GMOs). These and products derived from them must be subjected to all regulations of genetic engineering legislation.

Konventionelle Züchtungsmethoden und Mutationszüchtung (Auswahl)

Van de Weil C., Schaart J., Niks R. & Visser R. (2010): **Traditional plant breeding methods.** Wageningen UR Plant Breeding, Wageningen, May 2010 Report 338

Ahloowalia B., Maluszynski M. & Nichterlein K. (2004): **Global impact of mutation-derived varieties.** Euphytica 135, 187–204 | https://doi.org/10.1023/B:EUPH.0000014914.85465.4f

During the past seventy years, worldwide more than 2250 varieties have been released that have been derived either as direct mutants or from their progenies. Induction of mutations with radiation has been the most frequently used method for directly developed mutant varieties. The prime strategy in mutation-based breeding has been to upgrade the well-adapted plant varieties by altering one or two major traits, which limit their productivity or enhance their quality value. In this paper, the global impact of mutation-derived varieties on food production and quality enhancement is presented. In addition, the economic contribution of the selected mutant varieties of rice, barley, cotton, groundnut, pulses, sunflower, rapeseed and Japanese pear is discussed. In several mutation-derived varieties, the changed traits have resulted in synergistic effect on increasing the yield and quality of the crop, improving agronomic inputs, crop rotation, and consumer acceptance. In contrast to the currently protected plant varieties or germplasm and increasing restrictions on their use, the induced mutants have been freely available for plant breeding. Many mutants have made transnational impact on increasing yield and quality of several seed-propagated crops. Induced mutations will continue to have an increasing role in creating crop varieties with traits such as modified oil, protein and starch quality, enhanced uptake of specific metals, deeper rooting system, and resistance to drought, diseases and salinity as a major component of the environmentally sustainable agriculture. Future research on induced mutations would also be important in the functional genomics of many food crops.
https://link.springer.com/article/10.1023/B:EUPH.0000014914.85465.4f

Mutationszüchtungsdatenbank (FAO/IAEA Mutant Variety Database) der Internationalen Atomenergie-Organisation (IAEO) und der Ernährungs- und Landwirtschaftsorganisation der Vereinten Nationen (FAO)
Weltweit sind 3281 Pflanzen, die durch herkömmliche Mutationszüchtung erzeugt wurden, registriert. Insgesamt sind über 210 Pflanzenarten aus über 70 Ländern zugelassen; auf Deutschland entfallen dabei 172 Zulassungen.
https://mvd.iaea.org/

IAEA (1991): **Plant Mutation Breeding for Crop Improvement, Volume 2**
Proceedings of a symposium jointly organized by the IAEA and FAO, Vienna, 18–22 June 1990. The technology of mutation induction has been accepted by plant breeders as a valuable additional tool for creating improved cultivars for agriculture and horticulture. It was amply demonstrated at the symposium that this technique has been applied with great success in many annual seed propagated crops such as rice, barley, wheat, cotton, soybean and pea. The technological problems identified primarily concerned vegetatively propagated crops and, in general, the logistic difficulties in identifying desirable mutants in large mutagenized populations. Contents: (Vol. 2) Mutation breeding with particular objectives; Methodology of mutation breeding; Panel: Part 1: The role of plant breeding for the future of mankind and the need for genetic resources and opportunities for mutagenesis or gene engineering; Part 2: Plant mutation breeding: Its future role, the methodology needed, training and the research priorities.
https://www.iaea.org/publications/3711/plant-mutation-breeding-for-crop-improvement-volume-2

Pfenning M., Palfay G. & Guille T. (2008): **The CLEARFIELD® technology – A new broad-spectrum post-emergence weed control system for European sunflower growers**. Journal of Plant Diseases and Protection, Special Issue XXI, ISSN 1861-4051.
Sunflower (Helianthus annuus L.) is an important oilseed crop in Europe with a total planted area of about 9.2 million hectares in 2006. Weeds are a major production problem in sunflower cultivation. Sunflower is a poor competitor during the early growth stages until canopy closure. Therefore, weeds compete successfully during these growth stages for light, water and nutrients. Limitation of available herbicides, especially herbicides to control broadleaf weeds, causes considerable yield losses to sunflower producers. The CLEARFIELD technology has been developed in sunflower to allow the use of imidazolinone herbicides as a post-emergence weed control option. The mode of action of imidazolinone herbicides is the inhibition of the enzyme acetohydroxyacid synthase (AHAS). While conventional sunflower is sensitive to imidazolinone herbicides, CLEARFIELD sunflower hybrids have been modified to survive an otherwise lethal application of these herbicides. The trait for tolerance to imidazolinone herbicides in CLEARFIELD sunflower goes back to a naturally occurring mutation in the AHAS gene detected in a wild population of Helianthus annuus. This technology does not involve the introduction of foreign genetic material from other sources and thus is characterized as a non-GMO (genetically modified organism) process. CLEARFIELD herbicides provide exceptional foliar and soil activity to control a broad spectrum of weeds occurring across regions and cropping systems where sunflowers are produced.
http://www.ask-force.org/web/HerbizideTol/Pfenning-CLEARFIELD-technology-Sunflower-2008.pdf

Tan S. et al. (2005): **Imidazolinone-tolerant crops: history, current status and future**. Pest Management Science, 61: 246-257 - DOI: 10.1002/ps.993.
Imidazolinone herbicides, which include imazapyr, imazapic, imazethapyr, imazamox,imazamethabenz and imazaquin, control weeds by inhibiting the enzyme acetohydroxyacid synthase(AHAS), also called acetolactate synthase (ALS).AHAS is a critical enzyme for the biosynthesis of branched-chain amino acids in plants. Several variant AHAS genes conferring imidazolinone tolerance were discovered in plants through mutagenesis and selection, and were used to create imidazolinone-tolerant maize (Zea maysL), wheat (Triticum aestivumL), rice (Oryza sativaL), oilseed rape (BrassicanapusL) and sunflower (Helianthus annuusL). These crops were developed using conventional breeding methods and commercialized as Clearfield∗crops from 1992 to the present. Imidazolinone herbicides control a broad spectrum of grass and broadleaf weeds in imidazolinone-tolerant crops, including weeds that are closely related to the crop itself and some key parasitic weeds. Imidazolinone-tolerant crops may

also prevent rotational crop injury and injury caused by interaction between AHAS-inhibiting herbicides and insecticides. A single target-site mutation in the AHAS gene may confer tolerance to AHAS-inhibiting herbicides, so that it is technically possible to develop the imidazolinone-tolerance trait in many crops. Activities are currently directed toward the continued improvement of imidazolinone tolerance and development of new Clearfield∗crops. Management of herbicide-resistant weeds and gene flow from cropsto weeds are issues that must be considered with the development of any herbicide-resistant crop. Thus extensive stewardship programs have been developed to address these issues for Clearfield∗crops.
https://naldc.nal.usda.gov/download/6812/PDF

Tan S. and Bowe S.J. (2012): **Herbicide-tolerant crops developed from mutations.** *In* Plant mutation breeding and biotechnology, Eds Shu QY et al, ISBN 9781780640853
https://www.cabi.org/VetMedResource/ebook/20123349362

Vor EuGH Urteilsverkündung (nur Auswahl / Übersicht bei Ammann K.:(2018a)*

EU-Commission (1992): **Interpretation of the concept “Tradtitional Breeding” in the context of the exemptions outlined in Annexes I B of the Directives 90/219/EC and 90/220/EC.** DOC/XI/463/92fin
EU_Commission_1992_DOV_XI-463/92fin

Niederlande September 2017: In Bezug auf eine mögliche Regulation der neuen Züchtungstechniken in der EU ist der Vorstoß der Niederlande mit ihrem „Proposal for discussion on actions to improve the exemption mechanismn for genetically modified plants under Directive 2001/18“
Dieser Vorschlag wurde am 14.05. 2019 im Agrarrat diskutiert und 14 Mitgliedstaaten sprachen sich für eine Änderung/Anpassung der Gesetzgebung aus.
(s. auch https://www.biotech-gm-food.com/aktuelles/eu-agrarrat-befuerwortet-aenderungen-im-gentechnik-gesetz

High Level Group of Scientific Advisors / Scientific Advice Mechanism (SAM): Explanatory Notes 02/2017: **New techniques in Agricultural Biotechnology**
https://ec.europa.eu/research/sam/pdf/topics/explanatory_note_new_techniques_agricultural_biotechnology.pdf
This Explanatory Note on New Techniques in Agricultural Biotechnology (new breeding techniques) responds to a request made to the High Level Group of Scientific Advisors by Vytenis Andriukaitis, European Commissioner for Health and Food Safety. The Note provides a scientific and technical description of a wide range of breeding techniques used in agriculture in plants, animals and microorganisms, which are grouped under umbrella terms that reflect both historic and recent developments in breeding techniques, namely: conventional breeding techniques, established techniques of genetic modification, and new breeding techniques. The Note compares the various techniques according to a variety of criteria including: the maturity of the technique, the speed and cost with which the desired outcome can be achieved, and the ability to detect and identify changes in end products resulting from the employment of these techniques.
https://doi.org/10.2777/17902

Die Zusammenfassung auf den Seiten 17-24 gibt einen guten Überblick über den Inhalt der 168 Seiten umfassenden Publikation. Im SAM-Bericht werden ausdrücklich keine Aussagen zu einer möglichen gesetzlichen Einordnung der neuen Züchtungsmethoden gemacht.

Hier auch Statement nach den EuGH-Urteil:

A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive, November 2018
https://op.europa.eu/en/publication-detail/-/publication/a9100d3c-4930-11e9-a8ed-01aa75ed71a1/language-en/format-PDF/source-94584603

Callebaut, S., (2015), **New developments in modern biotechnology: A survey and analysis of the regulatory status of plants produced through New Breeding Techniques***,* Master Thesis, Faculty of Law Ghent University, Belgium.
https://lib.ugent.be/fulltxt/RUG01/002/213/647/RUG01-002213647_2015_0001_AC.pdf

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* Amman K. (2018a): Literature review: Modern Plant breeding and future biosafety regulation. Ask-Force No. 18 (updated)

Halford N.G. (2018): **Legislation governing genetically modified and genome-edited crops in Europe: the need for change.** Journal of the Science of Food and Agriculture | https://doi.org/10.1002/jsfa.9227
The European Commission's assessment and approval process for genetically modified (GM) crops has resulted in only two GM crop varieties being licensed for cultivation in the European Union, one of which has been withdrawn. Unable to define GM crops satisfactorily, the European Commission has fallen back on a definition based on process. The shortcomings of this approach are all too clear as the Commission grapples with the advent of genome editing. This has led to a long and damaging delay in the Commission issuing an opinion on how genome-edited crops should be regulated. At the same time, national bans imposed by member states on GM crops without any evidence of safety concerns have been legalized. The Commission also faces the prospect of assessing an increasing number of GM and genome-edited crops with deliberately altered composition. In this article, the operation of regulations covering GM crops in the European Union and the effect they have had on the development of plant biotechnology are reviewed, while the issues raised by new technologies are discussed. It is argued that there is an urgent need for the European Union to shift its position on plant biotechnology if agriculture is to meet the challenges of coming decades.
https://onlinelibrary.wiley.com/doi/epdf/10.1002/jsfa.9227

Robienski, J., Wasmer, M. (2018): **Produkte gezielter Mutagenese sind keine GVOs gemäß Art. 3 i.V.m. Anhang I B der Richtlinie 2001/18/EG.** *J Consum Prot Food Saf* **13,** 135–138 | https://doi.org/10.1007/s00003-017-1147-4
Die Europäische Richtlinie 2001/18/EG regelt die Freisetzung gentechnisch veränderter Organismen (GVO). Züchtungen mittels Mutagenese sind gemäß Art. 3 i.V.m. Anhang I B von der Richtlinie ausgenommen. Gilt diese Ausnahme nur für Produkte chemischer und strahleninduzierter Mutagenese oder auch für neue biotechnologische Verfahren gezielter Mutagenese? Unserer Analyse gemäß sind durch Mutagenese gewonnene Organismen von allen Regelungen der Richtlinie ausgenommen und fallen auch nicht in den Anwendungsbereich der Legaldefinition des Begriffs des genetisch veränderten Organismus im Sinne der Richtlinie. Der Begriff Mutagenese ist zudem dynamisch auszulegen, nach dessen naturwissenschaftlicher Bedeutung, welche auch gezielte Mutagenese umfasst. Dies bedeutet, dass Produkte gezielter Mutagenese keine GVOs im Sinne der Richtlinie sind.
The European Directive 2001/18/EC regulates the deliberate release of genetically modified organisms (GMO). Mutagenesis is excluded from the scope of the directive under Art. 3 and Annex I B. Does this exception only apply to products of chemical and radiation-induced mutagenesis or to new biotechnological methods of site-directed mutagenesis as well? In our opinion, organisms obtained by mutagenesis are generally exempted from all the provisions of the directive and are therefore also outside the scope of its legal definition of genetically modified organism. Furthermore, the term mutagenesis is to be interpreted dynamically, according to its meaning in science, which also includes site-directed mutagenesis. This means that in the sense of the directive, products of site-directed mutagenesis are not GMOs
https://link.springer.com/article/10.1007/s00003-017-1147-4

Wasmer, M., Robienski, J. (2018): **Which organisms and technologies fall under the mutagenesis exemption of the European GMO-Directive?.** *J Consum Prot Food Saf* **13,** 323–327 | https://doi.org/10.1007/s00003-018-1166-9 01.juni2018
The European GMO-Directive's (2001/18/EC) mutagenesis exemption may exempt organisms produced by genome editing from the legal obligations of the Directive, according to the recently published opinion of the Advocate General of the Court of Justice of the European Union (CJEU). We analyse his opinion and assess that the caveat in Art. 3(1) i.c.w. Annex 1B does not allow the use of nucleic acid vector constructs and CRISPR's sgRNA. This represents an obstacle for genome editing in plants and animals, since most current setups use vectors. However, alternatives are under way.
https://link.springer.com/article/10.1007/s00003-018-1166-9

Nach dem EuGH-Urteil:

Die Literatur ist alphabetisch geordnet und nicht nach Sachgebieten. Die Sammlung erhebt keinen Anspruch auf Vollständigkeit.

Agapito-Tenfen S.Z., Okoli A.S., Bernstein M.J., Wikmark O.-G. and Myhr AI (2018): **Revisiting Risk Governance of GM Plants: The Need to Consider New and Emerging Gene-Editing Techniques.** Front. Plant Sci. 9:1874. | doi: 10.3389/fpls.2018.01874
New and emerging gene-editing techniques make it possible to target specific genes in species with greater speed and specificity than previously possible. Of major relevance for plant breeding, regulators and scientists are discussing how to regulate products developed using these gene-editing techniques. Such discussions include whether to adopt or adapt the current framework for GMO risk governance in evaluating the impacts of gene-edited plants, and derived products, on the environment, human and animal health and society. Product classification or definition is one of several aspects of the current framework being criticized. Further, knowledge gaps related to risk assessments of gene-edited organisms—for example of target and off-target effects of intervention in plant genomes—are also of concern. Resolving these and related aspects of the current framework will involve addressing many subjective, value-laden positions, for example how to specify protection goals through ecosystem service approaches. A process informed by responsible research and innovation practices, involving a

broader community of people, organizations, experts, and interest groups, could help scientists, regulators, and other stakeholders address these complex, value-laden concerns related to gene-editing of plants with and for society.
https://www.frontiersin.org/articles/10.3389/fpls.2018.01874/full

Aerni P. (2019) **Politicizing the Precautionary Principle: Why Disregarding Facts Should Not Pass for Farsightedness.** Front. Plant Sci. 10:1053. doi: 10.3389/fpls.2019.0105
https://www.frontiersin.org/articles/10.3389/fpls.2019.01053/full

ALLEA: **Genome Editing for Crop Improvement**. ALLEA Symposium Report. October 2020.
allea.org/wp-content/uploads/2 … diting_Crop_2020.pdf DOI: 10.26356/gen-editing-crop

Ammann, K. (2019): **Innovative Solutions for the Regulation of GM crops in times of Gene Editing.** Ed. Dr. S. M. Paul Khurana & Dr. Rajarshi Kumar Gaur Springer International Publishing AG. Plant Biotechnology: Progress in Genomic Era, New York, 25 pp
http://www.ask-force.org/web/Rajastan/Ammann-Regulation-of-GM-crops-needs-Renovation-20191130-legaltext.pdf AND for private use full text citations
http://www.ask-force.org/web/Rajastan/Ammann-Regulation-of-GM-crops-needs-Renovation-20191130-fulltext.pdf open source

Andersen E. und Schreiber K. (2019**): Genome Editing“ vor dem EuGH und seine Folgen Eine Darstellung der durch das EuGH-Urteil C-528/16 hervorgerufenen Reaktionen.** Freiburger Informationspapiere zum Völkerrecht und Öffentlichen Recht. Silja Vöneky (Hrsg.) Ausgabe 11/2019
https://www.jura.uni-freiburg.de/de/institute/ioeffr2/downloads/online-papers/fip-11-2019

Andersen E. und Schreiber K. (2020): **„Genome Editing“ vor dem EuGH und seine Folgen.** NuR 42: 99–106
Der Beitrag untersucht die Reaktionen, die auf das EuGH-Urteil C-528/16 vom 25. 7. 2018 zur Anwendbarkeit der Europäischen Freisetzungsrichtlinie 2001/18/EG auf sogenannte Genomeditierungsverfahren im Rahmen der Grünen Gentechnologie erfolgt sind. Seit der Verkündung des Urteils im Juli 2018 wurde es umfassend und zum Teil auch höchst kritisch aus naturwissenschaftlicher, rechtswissenschaftlicher und wirtschaftlicher Perspektive beleuchtet und bewertet. Ziel dieses Beitrages ist es, einen Überblick über die unterschiedlichen Reaktionen zu geben und wesentliche Kritikpunkte aufzuzeigen. Damit soll die Bedeutung des Urteils im Rahmen der Diskussion um die Regulierung der Grünen Gentechnik eingeschätzt und bewertet werde
https://www.jura.uni-freiburg.de/de/institute/ioeffr2/downloads/forschung/cibss/andersen-schreiber-nur-2020-99

Andersen E. und Schreiber K. (2020): **Neue Regeln für die Gentechnik in Europa?** Eine Darstellung der faktischen Auswirkungen des EuGH-Urteils C-528/16 und der im Nachgang ergangenen Vorschläge für eine Reform des europäischen Gentechnikrechts. NuR 42,:168 –178, | https://doi.org/10.1007/s10357-020-3656-7
Das Urteil des EuGH in der Sache Confédération paysanne hat nicht nur Reaktionen im Hinblick auf die rechtliche Begründung und naturwissenschaftliche Nachvollziehbarkeit der Entscheidung hervorgerufen, sondern auch im Hinblick auf Auswirkungen des Urteils auf die Pflanzenbiotechnologie in Europa. Im Nachgang zur Entscheidung wird von Akteuren aus dem wissenschaftlichen und (wirtschafts-)politischen Bereich eine Reform des europäischen Gentechnikrechts gefordert. Diese Reformvorschläge werden abschließend dargestellt und diskutiert Zu Beginn ist festzuhalten, dass das EuGH-Urteil nur einen Anwendungsfall von Genomeditierungsverfahren betrifft, sog. neuartige, zielgerichtete Mutageneseverfah-ren.1 Ob diese in den Anwendungsbereich der Richtlinie 2001/18/EG über die absichtliche Freisetzung genetisch veränderter Organismen in die Umwelt (im Folgenden FreisetzungsRL) fallen, war vor der Entscheidung des EuGH strit-tig.3 Kennzeichnend für zielgerichtete Mutageneseverfahren ist, an einer zuvor bestimmten Stelle im Genom Mutationen hervorzurufen, ohne Fremd-DNA einzufügen. Dabei können unter anderem nur einzelne Basenpaare verändert wer-den.4 Der EuGH urteilte in seiner Entscheidung, dass das europäische Gentechnikrecht auf Pflanzen, die mit neuartigen Mutageneseverfahren erzeugt worden sind, anwendbar ist
https://link.springer.com/content/pdf/10.1007/s10357-020-3656-7.pdf

Anyshchenko, A. **The Precautionary Principle in EU Regulation of GMOs: Socio-Economic Considerations and Ethical Implications of Biotechnology**. Agric Environ Ethics | https://doi.org/10.1007/s10806-019-09802-2
Law is often linked to ethics and morality. Regulations of genetically modified organisms ensue from a discussion on how well the law is composed to accommodate ethical considerations. The precautionary principle and biotechnology have undeniable moral connotations. Besides, the principle has socio-economic implications. The application of the precautionary principle in plant breeding should be legally justified on the basis of the best available evidence. On the other hand, scientific information cannot provide all the necessary information on which a risk management decision should be based. This article addresses the issue of gap between science, ethics, and socio-economic considerations related to the cultivation and authorisation of GM crops.

https://link.springer.com/article/10.1007/s10806-019-09802-2

Australian Government- Department of Health: **Technical Review of the Gene Technology Regulations 2001**
Decision Regulation Impact Statement
http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/A0E750E72AC140C4CA2580B10011A68E/$File/Decision%20RIS.pdf

Baranski R., Klimek-Chodacka M., Lukasiewicz A. (2019): **Approved genetically modified (GM) horticultural plants: A 25-year perspective.** Folia Hort. 31(1), | DOI: 10.2478/fhort-2019-0001
In this review, we present genetically modified (GM) horticultural events that have passed the regulatory process and have been approved for cultivation or food use in different countries. The first authorization or deregulation of a GM horticultural plant issued 25 years ago initiated a fast expansion of GM organisms (GMO) engineered by using gene transfer technology. The list of GM horticultural species comprises representatives of vegetables, fruit plants and ornamentals. We describe their unique characteristics, often not achievable by conventional breeding, and how they were developed, and the approval process. Information on the adoption of GM horticultural cultivars and sale is accessed if commercialization has occurred. The review comprises, among others, Flavr SavrTM and other tomato cultivars with delayed ripening and improved shelf-life, insect-resistant eggplant (or brinjal), as well as virus-resistant squash, melon and the common bean, and also fruit trees, plum and papaya. Cultivation of the latter was particularly valuable to farmers in Hawaii as it ensured restoration of papaya production devastated earlier by the *Papaya ringspot virus* (PRSV). In contrast, a plum resistant to sharka (*Plum pox virus*; PPV) deregulated in the USA is still awaiting commercialization. GM events with improved quality include the recently marketed non-browning apple and high-lycopene pineapple. We also present orange petunia, blue 'Applause' rose and Moon-series carnations with a modified purple and violet flower colour. Finally, we discuss prospects of GM horticultural plants, including their development using promising new breeding technologies relying on genome editing and considered as an alternative to the transgenic approach.
https://content.sciendo.com/view/journals/fhort/31/1/article-p3.xml?language=en

Bartsch D, Ehlers U, Hartung F et al (2020): **Questions regarding the implementation of EU mutagenesis ruling in France**. Front Plant Sci. | https://doi.org/10.3389/fpls.2020.584485
The European Commission has asked EU Member States for comments on a French law notification demanding plant varieties produced with the help of *in vitro* mutagenesis have to be eliminated from the national catalog of approved varieties because of missing legal authorization deemed required by genetic engineering law. Primary target are herbicide-tolerant Clearfield oilseed rape varieties. The scientific reasoning is questionable, traceability is illusive, and law enforcement is likely to be impossible.
https://www.frontiersin.org/articles/10.3389/fpls.2020.584485/full

Bhattacharya A., Parkhi V. and Char B: (2020):**CRISPR/Cas Genome Editing - Strategies And Potential For Crop Improvement**
This book offers a comprehensive collection of papers on CRISPR/Cas genome editing in connection with agriculture, climate-smart crops, food security, translational research applications, bioinformatics analysis, practical applications in cereals, floriculture crops, engineering plants for abiotic stress resistance, the intellectual landscape, regulatory framework, and policy decisions.
Gathering contributions by internationally respected experts in the field of CRISPR/Cas genome editing, the book offers an essential guide for researchers, students, teachers and scientists in academia; policymakers; and public companies, private companies and cooperatives interested in understanding and/or applying CRISPR/Cas genome editing to develop new agricultural products.
https://link.springer.com/book/10.1007/978-3-030-42022-2

Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit (LGL-2019): Band 11 der Schriftenreihe Gentechnik für Umwelt- und Verbraucherschutz: **Genome Editing**
https://www.lgl.bayern.de/publikationen/doc/lgl_publikation_genome.pdf

Beck F. (2019): **All About That Risk? A (Re-)Assessment of the CJEU's Reasoning in the "Genome Editing" Case.** Zeitschrift für Europäisches Umwelt- und Planungsrecht 17 (2); 246 - 245
Der Europäische Gerichtshof hat mit Urteil vom 25.7.2018 (Rs. C-528/16) entschieden, dass Organismen, deren Erbgut mit Verfahren der sog. ortsspezifischen Mutagenese verändert wurde, dem europäischen Gentechnikrecht unterfallen. Die Entscheidung und ihre Konsequenzen sind seitdem Gegenstand reger Auseinandersetzungen. Pflanzenzüchter und große Teile der Wissenschaft kritisieren zu Recht die unreflektierte Feststellung des EuGH, mit der Genomeditierung seien ähnliche Risiken verbunden wie mit konventioneller Gentechnik. Der Beitrag untersucht insbesondere auch die juristischen Argumente der Entscheidung, die in der bisherigen Debatte erstaunlich geringe Aufmerksamkeit erfahren haben. Für die äußerst knappen Ausführungen des EuGH zum Vorsorgeprinzip wird ein Erklärungsansatz entwickelt. Entscheidend war aus Sicht des EuGH der 17. Erwägungsgrund der EU-Freisetzungsrichtlinie 2001/17/EG, dem zufolge nur solche Verfahren von der Regulierung ausgenommen werden sollen, die seit langem als sicher gelten. Dies kann auf die neuen Verfahren schon wegen des temporalen Elements nicht zutreffen, weshalb eine Risikobewertung letztlich hätte dahinstehen können. Im Ergebnis ist der

Entscheidung des EuGH jedoch zuzustimmen, denn es obliegt dem Gesetzgeber und nicht der Rechtsprechung, die Chancen und Risiken neuer Technologien abzuwägen und diese erforderlichenfalls einer sachgerechten Regulierung zu unterwerfen.
https://eurup.lexxion.eu/article/eurup/2019/2/13

Bertheau, Yves. (2019). **New Breeding Techniques: Detection and identification of the techniques and derived products.** In: Melton L et al (eds.) (2019). Encyclopedia of Food Chemistry. Reference Module in Food Science. Elsevier. 320-336. 10.1016/B978-0-08-100596-5.21834-9.
Since the commercial releases of GMOs in the 90s, new genetic modification tools known as New breeding techniques have been developed for e.g. gene silencing or more precise genomic modifications such as Crispr-endonuclease based systems. As for GMOs several consumers view may prevail about the societal interest in agricultural production and food of such genetic modification. Ensuring the freedom of choice to consumers needs to develop detection tools which could infer the NBT nature of the modification technique used. This article reviews all the elements which could allow the identification and detection of such techniques and products.
https://www.sciencedirect.com/science/article/pii/B9780081005965218349?via%3Dihub

BfR-Verbraucherkonferenz: **Verbrauchervotum:** Ergebnis der BfR-Verbraucherkonferenz „Genome Editing im Bereich Ernährung und menschliche Gesundheit“ 2019
https://www.bfr.bund.de/cm/343/verbrauchervotum-genome-editing.pdf

Bullock D.W., Wilson W.W., Neadeau J. (2021): **Gene editing versus genetic modification in research and development of new crop traits: An economic comparison.** Amer. J. Agr. Econ | https://doi.org/10.1111/ajae.12201
Gene editing is a relatively new plant-breeding tool that, unlike earlier methods such as genetic modification, is more precise in targeting its manipulations to site-specific locations within the genome. This precision with gene editing offers considerable research and development cost economies and a higher probability of success, particularly for the initial discovery phase of research and development. This study quantifies the advantages of gene editing versus genetic modification by examining the minimum required planted area for a proposed trait where a typical crop technology company can expect to break even on its research and development investment using a real option valuation model. A novel feature of the model is the combination of a decision tree with a binomial lattice for project valuation with an embedded abandonment real option. A primary numerical result from the model was the observation that gene editing required a much smaller potential market area (96% smaller) to break even on the financial investment when compared to genetic modification for the same trait value per acre. This result held across a wide range of potential trait values. Sensitivity analysis on the results indicated that the much higher probability of success for gene editing in the discovery phase of research and development was the primary driver of the difference in break-even acreage.
https://onlinelibrary.wiley.com/doi/10.1111/ajae.12201 pdf-file avaiable

Bundesministerium für Ernährung und Landwirtschaft (BMEL): **Neue molekularbiologische Techniken**
https://www.bmel.de/DE/Landwirtschaft/Pflanzenbau/Gentechnik/_Texte/Neue_molekularbiologische_Techniken.html

Gesetzliche Regelungen: https://www.bmel.de/SharedDocs/Downloads/Landwirtschaft/Pflanze/GrueneGentechnik/NMT_Stand-Regulierung_Anlage3.pdf;jsessionid=D5E4C6FDA0E250C24BD52227A207436F.2_cid385?__blob=publicationFile

Pflanzen: https://www.bmel.de/SharedDocs/Downloads/Landwirtschaft/Pflanze/GrueneGentechnik/NMT_Stand-Regulierung_Anlage4.pdf;jsessionid=D5E4C6FDA0E250C24BD52227A207436F.2_cid385?__blob=publicationFile

Tiere:
https://www.bmel.de/SharedDocs/Downloads/Landwirtschaft/Pflanze/GrueneGentechnik/NMT_Stand-Regulierung_Anlage5.pdf;jsessionid=D5E4C6FDA0E250C24BD52227A207436F.2_cid385?__blob=publicationFile

Übersicht über Nutz- und Zierpflanzen, die mit Hilfe der Gentechnik und neuer molekularbiologischer Techniken für die Bereiche Ernährung, Landwirtschaft, Gartenbau, Arzneimittelherstellung und -forschung entwickelt wurden.
https://www.bvl.bund.de/DE/06_Gentechnik/02_Verbraucher/09_Monitoring_Molekulare_Techniken/gentechnik_molekulare_techniken_node.html

Bogner A. and Torgersen H. (2018): **Precaution, Responsible Innovation and Beyond – In Search of a Sustainable Agricultural Biotechnology Policy**. Front. Plant Sci., 18 December 2018 | https://doi.org/10.3389/fpls.2018.01884
The recent ruling by the European Court of Justice on gene edited plants highlighted regulatory inadequacy as well as a decades-old political problem, namely how to reconcile diverging expectations regarding agricultural biotechnology in Europe. Over time, regulators had tried out various tools to address concerns and overcome implementation obstacles. While initially focussing on risk (with the Precautionary Principle), they later tried to

better embed technology in society (e.g., through Responsible Research and Innovation). The PP got criticized early-on; meanwhile, it seems to have lost much of its salience. Responsible Research and Innovation (RRI) is associated with problems of participation and political impact, often rendering it a public awareness tool only. We discuss problems with both approaches and conclude that also RRI falls short of facilitating technology implementation in the way regulators might have had in mind. Rather than leaving political decisions to technical risk assessment or ethics and public awareness, we argue for re-establishing a broad yet sober process of opinion formation and informed decision-making in agricultural policy.
https://www.frontiersin.org/articles/10.3389/fpls.2018.01884/full

Bratlie S. et al. (2019): **A novel governance framework for GMO**
A tiered, more flexible regulation for GMOs would help to stimulate innovation and public debate. EMBO reports 20: e47812 | https://doi.org/10.15252/embr.201947812
https://www.embopress.org/doi/abs/10.15252/embr.201947812

Broothaerts, W., Jacchia, S., Angers, A., Petrillo, M., Querci, M., Savini, C., Van den Eede, G. and Emons, H., **New Genomic Techniques: State-of-the-Art Review**, EUR 30430 EN, Publications Office of the European Union, Luxembourg, 2021, ISBN 978-92-76-24696-1, doi:10.2760/710056, JRC121847.
Since the adoption of Directive 2001/18 a variety of NGTs has been developed which are capable to alter the genome of an organism. These techniques aim to improve plant and animal breeding by accelerating the breeding process, and/or by rendering it more precise. They are seen as a promising field for the agri-food industry but they are offering also for the health industry great technical and innovative potential.This study used a systematic literature survey to identify the major NGTs employed for genome modifications in plants, animals and microorganisms.Many of the NGTs are built on the versatile CRISPR-Cas technology, which can be used in different versions and to which additional functionalities may be added.NGTs may affect only single nucleotide changes or may delete, replace or insert very large sequences and thus a classification of NGTs on the basis of the size of the nuclear fragment affected is not feasible.Here, we have therefore developed a classification system by arranging the NGTs into four groups based on the interaction of their active components with the genome. Furthermore, as a guidance to the regulator, we give an overview of the possible genome alterations and their likelihood of occurring in nature or through conventional breeding. We also provide the main NGTs that may be involved to generate those genome alterations in the different kingdoms of living organisms (bacteria, fungi, plants and animals). It must be noted that some NGTs may be used in combination with other NGTs for an improved performance
This review of the scientific and technological developments on New Genomic Techniques (NGTs) is aimed to provide the technical status of NGTs with respect to their diverse mechanisms of action and applicability. It has been compiled in support to the request to the Commission to submit a study in light of the Court of Justice's judgment in Case C-528/16 regarding the status of novel genomic techniques under Union law (Council Decision (EU) 2019/1904). Since the adoption of Directive 2001/18/EC a variety of NGTs has been developed which are capable to alter the genome of an organism. These techniques aim to modify plant, animal or microbial organisms by accelerating the breeding or development process, and/or by rendering it more precise. They are seen as promising instruments for the agri-food and industrial biotechnology sectors, but they are also offering tremendous innovative potential and technical possibilities for the health sector. This study used a systematic literature survey to identify the major NGTs employed for genome modifications in plants, animals and microorganisms. Many of the NGTs are built on the versatile CRISPR-Cas technology, which can be used in different versions and to which additional functionalities may be added. NGTs may affect only single nucleotide changes or may delete, replace or insert very large sequences and thus a classification of NGTs on the basis of the size of the nuclear fragment affected is not feasible. Here, we have therefore developed a classification system by arranging the NGTs into four groups based on the interaction of their active components with the genome. Furthermore, we give an overview of the possible genome alterations and their likelihood of occurring in nature or through conventional breeding. We also provide the main NGTs that may be involved to generate those genome alterations in the different kingdoms of living organisms (bacteria, fungi, plants and animals). It has to be noted that NGTs are continuously being modified for an improved performance and the field is still evolving in a very dynamic manner. Therefore, this review is providing a non-exhaustive list of NGTs without any implicit legal judgement on their status under current EU legislation.
https://publications.jrc.ec.europa.eu/repository/handle/JRC121847 here you can download the pfd-file

Bruetschy, C. The EU regulatory framework on genetically modified organisms (GMOs). *Transgenic Res* **28,** 169–174 (2019). https://doi.org/10.1007/s11248-019-00149-y
https://link.springer.com/article/10.1007/s11248-019-00149-y

BVL: **Überprüfung und Beurteilung der am 07.09.2020 veröffentlichten Nachweismethode für herbizidtoleranten Raps** (Chhalliyil et al., Foods 2020)
https://www.bvl.bund.de/SharedDocs/Downloads/06_Gentechnik/Ergebnisbericht_Ueberpr%C3%BCfung-und-Beurteilung-Nachweismethode-fuer-herbizidtoleranten-Raps.pdf;jsessionid=1E-ABADD978F344666AF5B5F4823A807A.2_cid360?__blob=publicationFile&v=4

Chimata M.K. & Bharti G. (2019): **Regulation of genome edited technologies in India.** Transgenic Res (2019) 28:175–181 | https://doi.org/10.1007/s11248-019-00148-z

In India, genetically modified organisms and products thereof are regulated under the "Rules for the manufacture, use, import, export and storage of hazardous microorganisms, genetically engineered organisms or cells, 1989" (referred to as Rules, 1989) notified under the Environment (Protection) Act, 1986. These Rules are implemented by the Ministry of Environment, Forest and Climate Change, Department of Biotechnology and State Governments though six competent authorities. The Rules, 1989 are supported by series of guidelines on contained research, biologics, confined field trials, food safety assessment, environmental risk assessment etc. The definition of genetic engineering in the Rules, 1989 implies that new genome engineering technologies including gene editing technologies like CRISPR/Cas9 and gene drives may be covered under the rules. The regulatory authorities if required, may also review the experiences of other countries in dealing with such new and emerging technologies.

https://link.springer.com/content/pdf/10.1007%2Fs11248-019-00148-z.pdf

Christiansen A. T., Andersen. M., Kappel K. (2019): **Are current EU policies on GMOs justified?** Transgenic Res. | https://doi.org/10.1007/s11248-019-00120-x

The European Court of Justice's recent ruling that the new techniques for crop development are to be considered as genetically modified organisms under the European Union's regulations exacerbates the need for a critical evaluation of those regulations. The paper analyzes the regulation from the perspective of moral and political philosophy. It considers whether influential arguments for restrictions of genetically modified organisms provide cogent justifications for the policies that are in place, in particular a pre-release authorization requirement, mandatory labelling, and de facto bans (in the form of withholding or opting out of authorizations). It is argued that arguments pertaining to risk can justify some form of pre-release authorization scheme, although not necessarily the current one, but that neither de facto bans nor mandatory labelling can be justified by reference to common arguments concerning naturalness, agricultural policy (in particular the promotion of organic farming), socio-economic effects, or consumers' right to choose.

https://link.springer.com/article/10.1007/s11248-019-00120-x pdf-file available

Cornelissen M., Małyska A., Nanda A.K., Lankhorst R.K. et al. (2020): **Biotechnology for Tomorrow's World: Scenarios to Guide Directions for Future Innovation.** Trends in Biotechnology | https://doi.org/10.1016/j.tibtech.2020.09.006

Depending on how the future will unfold, today's progress in biotechnology research has greater or lesser potential to be the basis of subsequent innovation. Tracking progress against indicators for different future scenarios will help to focus, emphasize, or de-emphasize discovery research in a timely manner and to maximize the chance for successful innovation. In this paper, we show how learning scenarios with a 2050 time horizon help to recognize the implications of political and societal developments on the innovation potential of ongoing biotechnological research. We also propose a model to further increase open innovation between academia and the biotechnology value chain to help fundamental research explore discovery fields that have a greater chance to be valuable for applied research.

https://www.cell.com/action/showPdf?pii=S0167-7799%2820%2930243-2

Cotter J., Kawall K., Then C. (2020): **New genetic engineering technologies**
https://www.testbiotech.org/sites/default/files/RAGES_report-%20new%20genetic%20engineering%20techniques.pdf

Custers R, Casacuberta JM, Eriksson D, Sági L and Schiemann J (2019) **Genetic Alterations That Do or o Not Occur Naturally; Consequences for Genome Edited Organisms in the Context of Regulatory Oversight**. Front. Bioeng. Biotechnol. 6: 213.
https://doi.org/10.3389/fbioe.2018.00213

The ability to successfully exploit genome edited organisms for the benefit of food security and the environment will essentially be determined by the extent to which these organisms fall under specific regulatory provisions. In many jurisdictions the answer to this question is considered to depend on the genetic characteristics of the edited organism, and whether the changes introduced in its genome do (or do not) occur naturally. We provide here a number of key considerations to assist with this evaluation as well as a guide of concrete examples of genetic alterations with an assessment of their natural occurrence. These examples support the conclusion that for many of the common types of alterations introduced by means of genome editing, the resulting organisms would not be subject to specific biosafety regulatory provisions whenever novelty of the genetic combination is a crucial determinant.

https://www.frontiersin.org/articles/10.3389/fbioe.2018.00213/full

Danisch council on ethics (2019): **Statement on GMO and ethics in a new ERA**
https://www.etiskraad.dk/~/media/Etisk-Raad/en/Publications/DCE_Statement_on_GMO_and_ethics_in_a_new_era_2019.pdf?la=da

Debode, F., Hulin, J., Charloteaux, B. et al. (2019): **Detection and identification of transgenic events by next generation sequencing combined with enrichment technologies**. Sci Rep 9**,** 15595 | https://doi.org/10.1038/s41598-019-51668-x

Next generation sequencing (NGS) is a promising tool for analysing the quality and safety of food and feed products. The detection and identification of genetically modified organisms (GMOs) is complex, as the diversity of transgenic events and types of structural elements introduced in plants continue to increase. In this paper, we show how a strategy that combines enrichment technologies with NGS can be used to detect a large panel of structural elements and partially or completely reconstruct the new sequence inserted into the plant genome in a single analysis, even at low GMO percentages. The strategy of enriching sequences of interest makes the approach applicable even to mixed products, which was not possible before due to insufficient coverage of the different genomes present. This approach is also the first step towards a more complete characterisation of agri-food products in a single analysis.
https://www.nature.com/articles/s41598-019-51668-x.pdf

Dederer H.- G. (2019): **Genomeditierung ist Gentechnik** Eine kritische Analyse des EuGH-Urteils Confédération paysanne u.a. Zeitschrift für Europäisches Umwelt- und Planungsrecht 17 (2); 236 - 245
On July 25, 2018, the Court of Justice of the European Union (CJEU), sitting in a Grand Chamber, rendered its highly controversial judgment in the case C-528/16, Confédération paysanne and Others. In light of the CJEU's reasoning, genome-edited organisms are, without exemption, genetically modified organisms (GMOs) within the meaning of Directive 2001/18/EC and, therefore, ultimately, governed by the EU's entire regulatory framework for GMOs. The fundamental source for an in-depth understanding of the Court's reasoning is not the Advocate General's opinion, which the Court blatantly dismissed, but the preliminary reference by the French Conseil d'État. In particular, the CJEU adopted the Conseil d'État's assumptions of risks arising allegedly from genome editing techniques, which, in turn, prompted the Court to apply the precautionary principle. The Court is to be criticized, inter alia, for not having impugned and scrutinized the alleged risks and for having applied the precautionary principle in disregard of its own case-law. Eventually, it is, by now, the Union legislator's task to decide on whether genome-edited organisms should be governed or, rather, exempted, at least in part, from the EU's legal framework on GMOs in order to avoid transatlantic trade conflicts and to ensure the competitivenes especially of small and medium-sized plant and animal breeders in Europe.
https://eurup.lexxion.eu/article/eurup/2019/2/12

Dederer H.- G., Hamburger D. (2019): **Regulation of Genome Editing in Plant Biotechnology**
A Comparative Analysis of Regulatory Frameworks of Selected Countries and the EU
Springer International Publishing : Print ISBN: 978-3-030-17118-6 / Electronic ISBN: 978-3-030-17119-3
This book provides in-depth insights into the regulatory frameworks of five countries and the EU concerning the regulation of genome edited plants. The country reports form the basis for a comparative analysis of the various national regulations governing genetically modified organisms (GMOs) in general and genome edited plants in particular, as well as the underlying regulatory approaches. The reports, which focus on the regulatory status quo of genome edited plants in Argentina, Australia, Canada, the EU, Japan and the USA, were written by distinguished experts following a uniform structure. On this basis, the legal frameworks are compared in order to foster a rational assessment of which approaches could be drawn upon to adjust, or to completely realign, the current EU regime for GMOs. In addition, a separate chapter identifies potential best practices for the regulation of plants derived from genome editing.
https://www.springerprofessional.de/regulation-of-genome-editing-in-plant-biotechnology/17076650

Department for Environment, Food and Rural Affairs (2021): **The regulation of genetic technologies -** A public consultation on the regulation of genetic technologies
https://consult.defra.gov.uk/agri-food-chain-directorate/the-regulation-of-genetic-technologies/supporting_documents/20210106%20Gene%20editing%20consultation%20document%20FINAL.pdf

Dima O., Inzé D. (2021): **The role of scientists in policy making for more sustainable agriculture.** Current Biology: 31(5): R218-R220 | DOI: 10.1016/j.cub.2021.01.090
https://www.cell.com/current-biology/fulltext/S0960-9822(21)00155-X?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS096098222100155X%3Fshowall%3Dtrue pdf-file available

Duensing, N., Sprink, T., Parrott, W. A., Fedorova, M., Lema, M. A., Wolt, J. D. and Bartsch, D. (2018): **Novel Features and Considerations for ERA and Regulation of Crops Produced by Genome Editing.** Front. Bioeng. Biotechnol. | https://doi.org/10.3389/fbioe.2018.00079
Genome editing describes a variety of molecular biology applications enabling targeted and precise alterations of the genomes of plants, animals and microorganisms. These rapidly developing techniques are likely to revolutionize the breeding of new crop varieties. Since genome editing can lead to the development of plants that could also have come into existence naturally or by conventional breeding techniques, there are strong arguments that these cases should not be classified as genetically modified organisms (GMOs) and be regulated no differently from conventionally bred crops. If a specific regulation would be regarded necessary, the application of genome editing for crop development may challenge risk assessment and post-market monitoring. In the session "Plant genome editing—any novel features to consider for ERA and regulation?" held at the 14th ISBGMO, scientists from various disciplines as well as regulators, risk assessors and potential users of the new technologies were brought together for a knowledge-based discussion to identify knowledge gaps and analyze scenarios for the

introduction of genome-edited crops into the environment. It was aimed to enable an open exchange forum on the regulatory approaches, ethical aspects and decision-making considerations.
https://www.frontiersin.org/articles/10.3389/fbioe.2018.00079/full

De Jong P., Bertolotto E. and De Seze I. (2018): **From farm to fork: the regulatory status of non-GMO plant innovations under current EU law.** BIO-SCIENCE LAW REVIEW 16 (3), 251-261
https://www.altius.com/images/Publications/De%20Jong/ARTICLE_-_de_Jong_et_al._-_From_farm_to_fork_BSLR_2018.pdf

Dumont P. (2021): **Regulatory approaches for genome-edited plants around the world**

1. Status of regulatory approaches for genome-edited plants
2. Is the AFBV-WGG initiative in harmony with regulatory systems outside Europe and the new European orientations?

► English-version ► German Version

Eckerstorfer M.F., Grabowski M., Lener M. , Engelhard M. (2021): **Biosafety of Genome Editing Applications in Plant Breeding: Considerations for a Focused Case-Specific Risk Assessment in the EU.** BioTech*,* 10 (3), 10 | https://doi.org/10.3390/biotech10030010
An intensely debated question is whether or how a mandatory environmental risk assessment (ERA) should be conducted for plants obtained through novel genomic techniques, including genome editing (GE). Some countries have already exempted certain types of GE applications from their regulations addressing genetically modified organisms (GMOs). In the European Union, the European Court of Justice confirmed in 2018 that plants developed by novel genomic techniques for directed mutagenesis are regulated as GMOs. Thus, they have to undergo an ERA prior to deliberate release or being placed on the market. Recently, the European Food Safety Authority (EFSA) published two opinions on the relevance of the current EU ERA framework for GM plants obtained through novel genomic techniques (NGTs). Regarding GE plants, the opinions confirmed that the existing ERA framework is suitable in general and that the current ERA requirements need to be applied in a case specific manner. Since EFSA did not provide further guidance, this review addresses a couple of issues relevant for the case-specific assessment of GE plants. We discuss the suitability of general denominators of risk/safety and address characteristics of GE plants which require particular assessment approaches. We suggest integrating the following two sets of considerations into the ERA: considerations related to the traits developed by GE and considerations addressing the assessment of method-related unintended effects, e.g., due to off-target modifications. In conclusion, we recommend that further specific guidance for the ERA and monitoring should be developed to facilitate a focused assessment approach for GE plants.
https://www.mdpi.com/2673-6284/10/3/10

Eckerstorfer M. F., Engelhard M., Heissenberger A., Samson Simon S., Teichmann H. (2019): **Plants Developed by New Genetic Modification Techniques—Comparison of Existing Regulatory Frameworks in the EU and Non-EU Countries.** Front. Bioeng. Biotechnol. | https://doi.org/10.3389/fbioe.2019.00026
The development of new genetic modification techniques (nGMs), also referred to as “new (breeding) techniques” in other sources, has raised worldwide discussions regarding their regulation. Different existing regulatory frameworks for genetically modified organisms (GMO) cover nGMs to varying degrees. Coverage of nGMs depends mostly on the regulatory trigger. In general two different trigger systems can be distinguished, taking into account either the process applied during development or the characteristics of the resulting product. A key question is whether regulatory frameworks either based on process- or product-oriented triggers are more advantageous for the regulation of nGM applications. We analyzed regulatory frameworks for GMO from different countries covering both trigger systems with a focus on their applicability to plants developed by various nGMs. The study is based on a literature analysis and qualitative interviews with regulatory experts and risk assessors of GMO in the respective countries. The applied principles of risk assessment are very similar in all investigated countries independent of the applied trigger for regulation. Even though the regulatory trigger is either process- or product-oriented, both triggers systems show features of the respective other in practice. In addition our analysis shows that both trigger systems have a number of generic advantages and disadvantages, but neither system can be regarded as superior at a general level. More decisive for the regulation of organisms or products, especially nGM applications, are the variable criteria and exceptions used to implement the triggers in the different regulatory frameworks. There are discussions and consultations in some countries about whether changes in legislation are necessary to establish a desired level of regulation of nGMs. We identified five strategies for countries that desire to regulate nGM applications for biosafety–ranging from applying existing biosafety frameworks without further amendments to establishing new stand-alone legislation. Due to varying degrees of nGM regulation, international harmonization will supposedly not be achieved in the near future. In the context of international trade, transparency of the regulatory status of individual nGM products is a crucial issue. We therefore propose to introduce an international public registry listing all biotechnology products commercially used in agriculture.
https://www.frontiersin.org/articles/10.3389/fbioe.2019.00026/full gute Übrsicht zu den Regelationen.

Eckerstorfer M.F., Heissenberger A.,.Reichenbecher W., Steinbrecher R.A. and Waßmann F. (2019): **An EU Perspective on Biosafety Considerations for Plants Developed by Genome Editing and Other New Genetic Modification Techniques (nGMs).** Front. Bioeng. Biotechnol. 7:31 | doi: 10.3389/fbioe.2019.00031

The question whether new genetic modification techniques (nGM) in plant development might result in non-negligible negative effects for the environment and/or health is significant for the discussion concerning their regulation. However, current knowledge to address this issue is limited for most nGMs, particularly for recently developed nGMs, like genome editing, and their newly emerging variations, e.g., base editing. This leads to uncertainties regarding the risk/safety-status of plants which are developed with a broad range of different nGMs, especially genome editing, and other nGMs such as cisgenesis, transgrafting, haploid induction or reverse breeding. A literature survey was conducted to identify plants developed by nGMs which are relevant for future agricultural use. Such nGMplants were analyzed for hazards associated either (i) with their developed traits and their use or (ii) with unintended changes resulting from the nGMs or other methods applied during breeding. Several traits are likely to become particularly relevant in the future for nGM plants, namely herbicide resistance (HR), resistance to different plant pathogens as well as modified composition, morphology, fitness (e.g., increased resistance to cold/frost, drought, or salinity) or modified reproductive characteristics. Some traits such as resistance to certain herbicides are already known from existing GM crops and their previous assessments identified issues of concern and/or risks, such as the development of herbicide resistant weeds. Other traits in nGM plants are novel; meaning they are not present in agricultural plants currently cultivated with a history of safe use, and their underlying physiological mechanisms are not yet sufficiently elucidated. Characteristics of some genome editing applications, e.g., the small extent of genomic sequence change and their higher targeting efficiency, i.e., precision, cannot be considered an indication of safety per se, especially in relation to novel traits created by such modifications. All nGMs considered here can result in unintended changes of different types and frequencies. However, the rapid development of nGM plants can compromise the detection and elimination of unintended effects. Thus, a case-specific premarket risk assessment should be conducted for nGM plants, including an appropriate molecular characterization to identify unintended changes and/or confirm the absence of unwanted transgenic sequences
https://www.frontiersin.org/articles/10.3389/fbioe.2019.00031/full

Eckerstorfer M., Dolezel M., Greiter A., Miklau M., Heissenberger A., Steinbrecher R. (2021): **Risk Assessment of Plants developed by new Genetic Modification Techniques (nGMs) Biosafety Considerations for Plants developed by Genome Editing and other new Genetic Modification Techniques (nGMs) and Considerations for their Regulation**
https://www.bfn.de/fileadmin/BfN/service/Dokumente/skripten/Skript592.pdf

Ehrenhofer-Murray A.: **Chance verpasst; ein rückwärtsgewandtes Urteil des EuGH zu Genom-editierten Organismen.**
Das Urteil wird klare negative Auswirkungen auf Forschung und Entwicklung in Europa haben. Dabei wäre gerade hier eine zukunftsorientierte Perspektive wünschenswert.
BioSpektrum 24(6):573-573, DOI: 10.1007/s12268-018-0959-9
http://link-springer-com-443.webvpn.jxutcm.edu.cn/content/pdf/10.1007%2Fs12268-018-0959-9.pdf

El-Mounadi K.,Morales-Floriano M.L., Garcia-Ruiz H. (2020): **Principles, Applications, and Biosafety of Plant Genome Editing Using CRISPR-Cas9.** Front. Plant Sci., | https://doi.org/10.3389/fpls.2020.00056

The terms genome engineering, genome editing, and gene editing, refer to modifications (insertions, deletions, substitutions) in the genome of a living organism. The most widely used approach to genome editing nowadays is based on Clustered Regularly Interspaced Short Palindromic Repeats and associated protein 9 (CRISPR-Cas9). In prokaryotes, CRISPR-Cas9 is an adaptive immune system that naturally protects cells from DNA virus infections. CRISPR-Cas9 has been modified to create a versatile genome editing technology that has a wide diversity of applications in medicine, agriculture, and basic studies of gene functions. CRISPR-Cas9 has been used in a growing number of monocot and dicot plant species to enhance yield, quality, and nutritional value, to introduce or enhance tolerance to biotic and abiotic stresses, among other applications. Although biosafety concerns remain, genome editing is a promising technology with potential to contribute to food production for the benefit of the growing human population. Here, we review the principles, current advances and applications of CRISPR-Cas9-based gene editing in crop improvement. We also address biosafety concerns and show that humans have been exposed to Cas9 protein homologues long before the use of CRISPR-Cas9 in genome editing.
https://www.frontiersin.org/articles/10.3389/fpls.2020.00056/full

Emons H., Broothaerts W., Bonfini L., Corbisier P., Gatto F., Jacchia S., Mazzara M., Savini C., **Challenges for the detection of genetically modified food or feed originating from genome editing,** EUR 29391 EN, Publications Office of the European Union, Luxembourg, 2018, ISBN 978-92-79-96398-8, doi:10.2760/732526

The recent ruling of the European Court of Justice has confirmed that organisms obtained by mutagenesis techniques are genetically modified organisms (GMOs). However, in contrast to organisms originating from conventional mutagenesis techniques, those obtained by new mutagenesis techniques are not exempted from the ob-

ligations of the GMO EU regulatory framework. This ruling raises questions about the detectability of the corresponding GM food and feed products. A case study is used in this document to explain and discuss possibilities and limitations for the detection and quantification of (known and unknown) genetic modifications in plant products derived from new mutagenesis techniques. Many of the mutations induced by new mutagenesis techniques cannot be unequivocally distinguished from natural mutations because such genome editing technologies are able to create very precise and limited genome changes that mimic the result of potential naturally occurring mutations. Moreover, mutations obtained by genome editing technologies could also not be differentiated from those introduced by conventional mutagenesis techniques which have been incorporated in traditional breeding programs and are often not thoroughly documented. Products of genome editing could only be detected and identified in imports of commodity products by enforcement laboratories when prior knowledge on the altered genome sequence, a validated detection method with appropriate selectivity and certified reference materials are available, similarly as required for the authorisation of current transgenic GMOs. However, when the modification involves only a SNP or few nucleotide changes, it would not be possible to identify whether the mutation originated spontaneously or was induced by conventional or new (genome editing) mutagenesis techniques. Moreover, it is unlikely that methods for the quantification of GMO products with small genome modifications in complex food or feed materials provide the level of selectivity needed for the enforcement of legislation, such as the one on labelling. In the absence of prior knowledge on the genome-edited changes, it is likely that non-authorised genetically modified food and feed products obtained by genome editing would enter the EU market undetected. The EU control system for GMOs and corresponding food and feed products may not function as efficiently for unauthorised genome-edited products compared to transgenic GMOs. In particular, the principle of zero tolerance for unauthorised GMO on the EU market is more difficult to maintain.
https://www.infogm.org/IMG/pdf/comeur_note-detection-nveaux-ogm_nov2018.pdf

Entine, J., Felipe, M.S.S., Groenewald, JH. et al. (2021): **Regulatory approaches for genome edited agricultural plants in select countries and jurisdictions around the world.** Transgenic Res | https://doi.org/10.1007/s11248-021-00257-8

Genome editing in agriculture and food is leading to new, improved crops and other products. Depending on the regulatory approach taken in each country or region, commercialization of these crops and products may or may not require approval from the respective regulatory authorities. This paper describes the regulatory landscape governing genome edited agriculture and food products in a selection of countries and regions. Significance statement: Genome editing techniques are rapidly being developed and applied to serve agricultural and food production objectives. In order to benefit fully, products developed using GEd must face reasonable, science-based safety regulations. This is particularly true of commodity crops, considering the proportion of such crops in international trade, and the prospect of their being subject to multiple, inconsistent and non-science based regulations as they traverse different jurisdictions. GEd crops developers need to be aware of the mosaic of regulations and regulatory schemes their products will have to pass prior to commercial release; this paper provides a glimpse of the varied approaches taken to regulating GEd crops in several jurisdictions around the world. For additional information, including ancillary data from several countries, the reader is directed to the Supplementary on line information accompanying this article. This article originally included a section on the EU, but revisions to that section were judged to be unacceptable by reviewers, who recommended rejection of the entire manuscript. In order to enable publication of the rest of the manuscript, the EU section was regrettably removed.
Paul Christou, *University of Lleida-Agrotecnio CERCA Center, Lleida, Spain and ICREA, Barcelona, Spain.*
https://link.springer.com/content/pdf/10.1007/s11248-021-00257-8.pdf

Eş I., M. Gavahian M., F.J. Marti-Quijal F.J. et al. (2019): **The application of the CRISPR-Cas9 genome editing machinery in food and agricultural science: Current status, future perspectives, and associated challenges.** Biotechnology Advances | https://doi.org/10.1016/j.biotechadv.2019.02.006

The recent progress in genetic engineering has brought multiple benefits to the food and agricultural industry by enhancing essential characteristics of agronomic traits. Powerful tools in the field of genome editing, such as siRNA mediated RNA interference for targeted suppression of gene expression and transcription activator-like effector nucleases (TALENs) and zinc-finger nucleases (ZFNs) for DNA repair have been widely used for commercial purposes. However, in the last few years, the discovery of the CRISPR-Cas9 system has revolutionized genome editing and has attracted attention as a powerful tool for several industrial applications. Herein, we review current progresses in the utilization of the CRISPR-Cas9 system in the food and agricultural industry, particularly in the development of resistant crops with improved quality and productivity. We compare the CRISPR system with the TALEN and ZFN nucleases–based methods and highlight potential advantages and shortcomings. In addition, we explore the state of the global market and discuss the safety and ethical concerns associated with the application of this technology in the food and agricultural industry.
https://www.sciencedirect.com/science/article/pii/S0734975019300254?via%3Dihub

Eriksson, D. (2018): **Recovering the Original Intentions of Risk Assessment and Management of Genetically Modified Organisms in the European Union.** Front. Bioeng. Biotechnol.| https://doi.org/10.3389/fbioe.2018.00052
https://www.frontiersin.org/articles/10.3389/fbioe.2018.00052/full
http://www.ask-force.org/web/Regulation/Eriksson-Recovering-Original-Intentions-Risk-Assessment-2018.pdf

Eriksson D.; Kershen D.; Nepomuceno A., Pogson P.J., Prieto H., Purnhagen K., Smyth S., Wesseler J, Whelan A. (2018): **A comparison of the EU regulatory approach to directed mutagenesis with that of other jurisdictions, consequences for international trade and potential steps forward.** New Phytologist: https://doi.org/10.1111/nph.15627

A special regulatory regime applies to products of recombinant nucleic acid modifications. A ruling from the European Court of Justice has interpreted this regulatory regime in a way that it also applies to emerging mutagenesis techniques. Elsewhere regulatory progress is also ongoing. In 2015, Argentina launched a regulatory framework, followed by Chile in 2017 and recently Brazil and Colombia. In March 2018, the USDA announced that it will not regulate genome-edited plants differently if they could have also been developed through traditional breeding. Canada has an altogether different approach with their Plants with Novel Traits regulations. Australia is currently reviewing its Gene Technology Act. This article illustrates the deviation of the EU's approach from the one of most of the other countries studied here. Whereas the EU does not implement a case-by-case approach, this approach is taken by several other jurisdictions. Also, the EU court ruling adheres to a process-based approach while most other countries have a stronger emphasis on the regulation of the resulting product. It is concluded that, unless a functioning identity preservation system for products of directed mutagenesis can be established, the deviation results in a risk of asynchronous approvals and disruptions in international trade.
https://nph.onlinelibrary.wiley.com/doi/epdf/10.1111/nph.15627

Eriksson D. et al. (2019): **Implementing an EU opt-in mechanism for GM crop cultivation**. *EMBO Reports* e48036 DOI 10.15252/embr.201948036

http://embor.embopress.org/content/early/2019/04/23/embr.201948036.abstract

https://rdcu.be/bAUgb

see also: Eriksson D et al (2018). Why the European Union needs a national GMO opt-in mechanism. Nature Biotechnology, 36(1): 18-19.
https://www.nature.com/articles/nbt.4051.epdf?author_access_token=UfZ7MitzPnJ1dvJ-INWa5NRgN0jA-jWel9jnR3ZoTv0MFsq86wiIDO_37PLUKbKT08NtCQdu6y2BZUvh8JqF48qX5nOUAC6xjzB5PE8pFl8WtINaRxl-iDEIJ9xOxGgVoM

Eriksson D. (2019): **The evolving EU regulatory framework for precision breeding**. Theoretical and Applied Genetics (2019) 132:569–573 | https://doi.org/10.1007/s00122-018-3200-9

Plant breeding has always relied on progress in various scientific disciplines to generate and enable access to genetic variation. Until the 1970s, available techniques generated mostly random genetic alterations that were subject to a selection procedure in the plant material. Recombinant nucleic acid technology, however, started a new era of targeted genetic alterations, or precision breeding, enabling a much more targeted approach to trait management. More recently, developments in genome editing are now providing yet more control by enabling alterations at exact locations in the genome. The potential of recombinant nucleic acid technology fuelled discussions about potentially new associated risks and, starting in the late 1980s, biosafety legislation for genetically modified organisms (GMOs) has developed in the European Union. However, the last decade has witnessed a lot of discussions as to whether or not genome editing and other precision breeding techniques should be encompassed by the EU GMO legislation. A recent ruling from the Court of Justice of the European Union indicated that directed mutagenesis techniques should be subject to the provisions of the GMO Directive, essentially putting many precision breeding techniques in the same regulatory basket. This review outlines the evolving EU regulatory framework for GMOs and discusses some potential routes that the EU may take for the regulation of precision breeding.
https://link.springer.com/content/pdf/10.1007%2Fs00122-018-3200-9.pdf
http://www.ask-force.org/web/Genomics/Eriksson-Evolving-EU-regulatory-framework-precision-breeding-2018.pdf

Eriksson D., Custers R., Björnberg K. E. et al. (2020): **Options to Reform the European Union Legislation on GMOs: Scope and Definitions.** Trends in Biotechnology, 38 (3), 231-234 |DOI: https://doi.org/10.1016/j.tibtech.2019.12.002

We discuss options to reform the EU genetically modified organisms (GMO) regulatory framework, make risk assessment and decision-making more consistent with scientific principles, and lay the groundwork for international coherence. The first in a three-part series, this article focuses on re-form options related to the scope of the legislation and the GMO definition.
https://www.cell.com/action/showPdf?pii=S0167-7799%2819%2930295-1

Eriksson D., Custers R., Björnberg K. E. et al. (2020): **Options to Reform the European Union Legislation on GMOs: Risk Governance**
Trends in Biotechnology, 38 (3) | DOI:https://doi.org/10.1016/j.tibtech.2019.12.016

Here, we discuss options to reform the EU genetically modified organ-ism (GMO) regulatory framework,to make risk assessment and decision-making more consistent with scientific principles, and to lay the groundwork for international coherence. We discussed the scope and definitions in a previous article and, thus, here we focus on the procedures for risk assessment and risk management.
https://www.cell.com/action/showPdf?pii=S0167-7799%2819%2930311-7

Eriksson D., Custers R., Björnberg K. E. et al. (2020): **Options to Reform the European Union Legislation on GMOs: Post-authorization and Beyond.** Trends in Biotechnology, 38 (3) | DOI: https://doi.org/10.1016/j.tibtech.2019.12.015
We discuss options to reform theEU genetically modified organism (GMO) regulatory framework, make risk assessment and decision-making more consistent with scientific principles, and lay the ground-work for international coherence. In this third of three articles, we focus on labeling and coexistence as well as discuss the political reality and potential ways forward.
https://www.cell.com/action/showPdf?pii=S0167-7799%2819%2930310-5

Eriksson, D., Zimny, T. (2020): **Critical observations on the French Conseil d'État ruling on plant mutagenesis.** *Nat. Plants* 6**,** 1392–1393 | https://doi.org/10.1038/s41477-020-00819-4
https://www.nature.com/articles/s41477-020-00819-4

European Network of GMO Laboratories (ENGL): **Detection of food and feed plant products obtained by new mutagenesis techniques**
https://gmo-crl.jrc.ec.europa.eu/doc/JRC116289-GE-report-ENGL.pdf

European Network of GMO Laboratories (ENGL): **Evaluation of the scientific publication: "A Real-Time Quantitative PCR Method Specific for Detection and Quantification of the First Commercialized Genome-Edited Plant"** P. Chhalliyilet al. in: Foods (2020) 9, 1245
https://gmo-crl.jrc.ec.europa.eu/ENGL/docs/ENGL%20Evaluation%20of%20the%20scientific%20publication%2002-10-2020.pdf

European Group on Ethics in Science and New Technologies - **Opinion on Ethics of Genome Editing**
https://ec.europa.eu/info/files/ethics-genome-editing_en

Faltus T. (ed) (2020): **Ethik, Recht und Kommunikation des Genome Editings**
Die Beiträge dieser Publikation entstanden im Rahmen des vom BMBF geförderten Verbundforschungsprojekts „GenomELECTION: Genomeditierung –ethische, rechtliche und kommunikationswissenschaftliche Aspekte im Bereichder molekularen Medizin und Nutzpflanzenzüchtung", Förderkennzeichen01GP1614A (ethischer und rechtswissenschaftlicher Projektteil, jeweils Martin-Luther-Universität Halle-Wittenberg) & Förderkennzeichen 01GP1614B(kommunikationswissenschaftlicher Projektteil, Museum für Naturkunde Berlin)
https://uvhw.de/download/978-3-86977-202-8.pdf

Faltus T. (2018): **Das Mutagenese-Urteil des EuGH schwächt die rechtssichere Anwendung der Gentechnik.** ZUR 10, 524
Mit Urteil vom 25.7.2018 in der Rechtssache C-528/16 hat der EuGH entschieden, dass alle mit Verfahren der Mutagenese gewonnenen Organismen genetisch veränderte Organismen (GVOs) im Sinne der EU-Freisetzungs-richtlinie 2001/18/EG sind. Zudem hat der EuGH entschieden, dass die Mutageneseausnahme der Freisetzungs-richtlinie, die zu einem Anwendungsausschluss die Richtlinie führt, nur für die Mutageneseverfahren gilt, die bis zum Erlass der Richtlinie etabliert waren. Daher werden die GVOs vom Anwendungsbereich der Richtlinie erfasst, die durch neuere Mutageneseverfahren erzeugt worden sind; unabhängig von deren höheren Genauigkeit und besseren Steuerbarkeit im Vergleich zu den älteren Verfahren. Der EuGH hat im Rahmen seines Mutagenese-Urteils allerdings den naturwissenschaftlich-technischen Kenntnisstand fehlerhaft rezipiert und vor allem Anreize für eine proaktive Umgehung seiner Rechtsprechung in Bezug auf neue Verfahren der Mutagenese, wozu auch die Methoden der Genomeditierung verwendet werden können, geschaffen.
https://beck-online.beck.de/Bcid/Y-300-Z-ZUR-B-2018-S-524-N-1

Friedrichs S. et al. (2019): **An overview of regulatory approaches to genome editing in agriculture.** Biotechnology Research and Innovation (2019), | https://doi.org/10.1016/j.biori.2019.07.001
The "OECD Conference on Genome Editing: Applications in Agriculture – Implications for Health, Environment and Regulation", brought together policy makers, academia, innovators and other stakeholders involved in the topic, in order to take stock of the existing research and applications of genome editing, and to thereby provide science-based input to the discussion of the potential impact of genome editing in the context of overarching agricultural and food policies. The conference provided a timely opportunity for information exchange between scientific experts, risk assessors, policy makers, regulators, private sector innovators and other stakeholders from around the world. In this paper, we summarise the conference session on the "Regulatory aspects" concerning genome editing (Session 3), during which government representatives from six different countries around the world reported on the policy frameworks pertaining to genome editing in their respective countries, and discussed their specificities, as well as the common issues
https://reader.elsevier.com/reader/sd/pii/S2452072119300371?token=AA81A40E449D911B062CA21F135D41677624AC37E66C297383FBD7B8732867E2A539ABB8C1CAFD6E5C948966D8BFB859

Friedrichs, S., Takasu, Y., Kearns, P. et al. **Meeting report of the OECD conference on "Genome Editing: Applications in Agriculture—Implications for Health, Environment and Regulation"** Transgenic Res (2019) 28: 419-463 | https://doi.org/10.1007/s11248-019-00154-1

The "OECD Conference on Genome Editing: Applications in Agriculture—Implications for Health, Environment and Regulation" was held on the 28–29 June 2018 at the OECD headquarter and conference centre in Paris, France. It brought together policy makers, academia, innovators and other stakeholders involved in the topic, in order to take stock of the current technical developments and implementations of genome editing, as well as their applications in various areas of agriculture and the implications they give rise to (More information on the "OECD Conference on Genome Editing: Applications in Agriculture—Implications for Health, Environment and Regulation" can be found on the OECD Genome Editing hub: http://www.oecd.org/environment/genome-editing-agriculture/; the hub also contains the detailed conference programme, the biographies of all conference speakers, the detailed conference abstracts, and the presentations of the two-day conference). The conference aimed to provide a clearer understanding of the regulatory considerations raised by products of genome editing, pointing towards a coherent policy approach to facilitate innovations involving genome editing.

https://link.springer.com/article/10.1007%2Fs11248-019-00154-1

https://link.springer.com/content/pdf/10.1007%2Fs11248-019-00154-1.pdf

Friedrichs S., Takasu Y., Kearns P., Dagallier B., Oshima R., Schofield J., Moreddu C. (2019): **Policy Considerations Regarding Genome Editing.** Trends Biotechnol. pii: S0167-7799(19)30112-X. | doi: 10.1016/j.tibtech.2019.05.005.

The international Organisation for Economic and Co-operative Development (OECD) conference on genome editing (June 2018) provided a timely platform for scientists, risk assessors, policy-makers, and regulators to discuss the applications and implications of this technology in various agriculture areas and the related policy considerations; in addition questions related to appropriate safety assessments and the regulation of genome-edited products were debated.

https://www.sciencedirect.com/science/article/abs/pii/S016777991930112X

Fritsche S., Poovaiah C., MacRae E. and Thorlby G. (2018): **A New Zealand Perspective on the Application and Regulation of Gene Editing.** Front. Plant Sci., 12 September 2018 | https://doi.org/10.3389/fpls.2018.01323

New Zealand (NZ) is a small country with an export-led economy with above 90% of primary production exported. Plant-based primary commodities derived from the pastoral, horticultural and forestry sectors account for around half of the export earnings. Productivity is characterized by a history of innovation and the early adoption of advanced technologies. Gene editing has the potential to revolutionize breeding programmes, particularly in NZ. Here, perennials such as tree crops and forestry species are key components of the primary production value chain but are challenging for conventional breeding and only recently domesticated. Uncertainty over the global regulatory status of gene editing products is a barrier to invest in and apply editing techniques in plant breeding. NZs major trading partners including Europe, Asia and Australia are currently evaluating the regulatory status of these technologies and have not made definitive decisions. NZ is one of the few countries where the regulatory status of gene editing has been clarified. In 2014, the NZ Environmental Protection Authority ruled that plants produced via gene editing methods, where no foreign DNA remained in the edited plant, would not be regulated as GMOs. However, following a challenge in the High Court, this decision was overturned such that NZ currently controls all products of gene editing as GMOs. Here, we illustrate the potential benefits of integrating gene editing into plant breeding programmes using targets and traits with application in NZ. The regulatory process which led to gene editing's current GMO classification in NZ is described and the importance of globally harmonized regulations, particularly to small export-driven nations is discussed.

https://www.frontiersin.org/articles/10.3389/fpls.2018.01323/full

Gabrielczyk T. **Council presses EC to decide on genome editing.** European Biotechnology – winter edition Vol 18 (2019)

Modern breeding Techniques: After years of regulatory deadlock concerning political decision making on genome-edited and genetically targeted mutational breeding, the European council has demanded that the European commission regulate new plant breeding techniques (NBT), such as oligonucleotid-directed mutagenesis (ODM), gene scissors (CRISPR), and others.

Gabrielczyk T. (2018): **CJEU ruling triggers exodus of EU plant research.** European Biotechnology 17

According to a brand-new EU-wide survey, European plant researchers are concerned about the European Court of Justice's (CJEU) interpretation that targeted mutation methods aimed at improving crop yield and resistance to climate change yield GMOs. In an open letter, they call for political action and a modernisation of the EU Directive 2001/18/EC because a lack in tech-transfer would put Europe at the bottom of the pile in the upcoming bioeconomy.

https://european-biotechnology.com/the-mag/issues/issue/cjeu-ruling-triggers-exodus-of-eu-plant-research.html

Gao C. (2019): **Precision plant breeding using genome editing technologies.** Transgenic Res (2019) 28:53–55 | https://doi.org/10.1007/s11248-019-00132-7

https://link.springer.com/article/10.1007/s11248-019-00132-7

Gao C.: (2020): **Genome engineering for crop improvement and future agriculture.** Cell | DOI:https://doi.org/10.1016/j.cell.2021.01.005
Feeding the ever-growing population is a major challenge, especially in light of rapidly changing climate conditions. Genome editing is set to revolutionize plant breeding and could help secure the global food supply. Here, I review the development and application of genome editing tools in plants while highlighting newly developed techniques. I describe new plant breeding strategies based on genome editing and discuss their impact on crop production, with an emphasis on recent advancements in genome editing-based plant improvements that could not be achieved by conventional breeding. I also discuss challenges facing genome editing that must be overcome before realizing the full potential of this technology toward future crops and food production.
https://www.cell.com/cell/pdf/S0092-8674(21)00005-2.pdf

Garnett (2019): **Hold your pipettes: *The European Court of Justice's findings in Confédération Paysanne & Others stirs GMOtions.*** RECIEL. 2019;00:1–7. | https://doi.org/10.1111/reel.12291
In July 2018, the Court of Justice of the European Union (CJEU) gave its final ruling on the much anticipated Confédération Paysanne & Others case on the regulation of mutagenic plants in the European Union (EU). Advocate General Bobek had opined that mutagenic techniques for the development of novel plant varieties should be ex- empted from the stringent provisions set out in the EU genetically modified organisms (GMO) Directive. It came as somewhat of a surprise, therefore, when the Court of Justice, in its final ruling, took a diametrically opposite point of view to that of the Advocate General, and concluded that novel mutagenic techniques must be subject to the provisions set out in the EU's various regulations relating to GMOs. The scientific community are now calling for the European Commission to consider new legislation to take account of novel plant breeding techniques. This case note sets out how the CJEU reached its conclusions, explains why the GMO Directive is not anti-science and considers the important role that defining 'natural' within a legal context will play in the forthcoming debate on science, innovation and novel plant breeding techniques.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/reel.12291

Gatica-Arias A. (2020): **The regulatory current status of plant breeding technologies in some Latin American and the Caribbean countries**. Plant Cell, Tissue and Organ Culture (PCTOC) | https://doi.org/10.1007/s11240-020-01799-1
Precision biotechnologies have appeared on the horizon resulting in a plethora of possibilities to modify the genome of different organisms with relatively easy application, low cost, and high precision. These technologies make it possible to work with a very simple biological system and have great potential for medicine, and agriculture. Latin American is embracing the technology and researchers are already developing tropical products from its use. The following article explains the operation of these technologies, and some considerations about its regulation among counties in Latin America and the Caribbean region. Survey results demonstrated that seven countries (Argentina, Brazil, Colombia, Chile, Guatemala, Honduras, and Paraguay) have a clearly defined and operational legal framework for new breeding technologies. Nevertheless, the majority of countries in the region have no experience regarding these technologies and lack legal clarity. Therefore, these countries require regulatory clarity to legally differentiate those products of gene editing that are comparable to conventional breeding and those that can be legally defined as a genetically modified organism.
https://link.springer.com/article/10.1007%2Fs11240-020-01799-1

Gelinsky E. and Hilbeck A. (2018): **European Court of Justice ruling regarding new genetic engineering methods scientifically justified: a commentary on the biased reporting about the recent ruling.** Environmental Sciences Europe **30**: 52; https://doi.org/10.1186/s12302-018-0182-9
In July 2018, the European Court of Justice (Case C-528/16) ruled that organisms obtained by directed mutagenesis techniques are to be regarded as genetically modified organisms (GMOs) within the meaning of Directive 2001/18. The ruling marked the next round of the dispute around agricultural genetic engineering in Europe. Many of the pros and cons presented in this dispute are familiar from the debate around the first generation of genetic engineering techniques. The current wave of enthusiasm for the new genetic engineering methods, with its claim to make good on the failed promises of the previous wave, seems to point more to an admission of failure of the last generation of genetic engineering than to a true change of paradigm. Regulation is being portrayed as a ban on research and use, which is factually incorrect, and the judges of the European Court of Justice are being defamed as espousing "pseudoscience". Furthermore, this highly polarised position dominates the media reporting of the new techniques and the court's ruling. Advocates of the new genetic engineering techniques appear to believe that their benefits are so clear that furnishing reliable scientific evidence is unnecessary. Meanwhile, critics who believe that the institution of science is in a serious crisis are on the increase not just due to the cases of obvious documented scientific misconduct by companies and scientists, but also due to the approach of dividing the world into those categorically for or against genetic engineering. In this construct of irreconcilable opposites, differentiations fall by the wayside. This article is a response to this one-sided and biased reporting, which often has the appearance of spin and lacks journalistic ethics that require journalists to report on different positions in a balanced and factual manner instead of taking positions and becoming undeclared advocates themselves.
https://enveurope.springeropen.com/articles/10.1186/s12302-018-0182-9
https://enveurope.springeropen.com/track/pdf/10.1186/s12302-018-0182-9

https://ensser.org/publications/publications_2018/einseitige-angriffe-und-eine-voreingenommene-berichterstattung-zum-eugh-urteil-uber-neue-gentechnikmethoden-entlarven-ein-anmassendes-und-unaufgeklartes-wissenschafts-demokratie-und-rechtsverstandni/

Gelinsky E. (2021): **Warten auf Superpflanzen?** CRISPR & Co wecken übertriebene Erwartungen
In: ABL: **Neue Gentechnik Regulierung oder Freifahrtschein?** Texte zur aktuellen Diskussion
http://abl-ev.de/fileadmin/Dokumente/AbL_ev/Publikationen/AbL_CRISPR___CO_Neue_Gentechnik_-_Regulierung_oder_Freifahrtschein_WEB6_vorab.pdf

Girnau, M. (2019): **Die Auswirkungen des EUGH-Urteils zu neuen Züchtungstechniken auf das Lebensmittelrecht.** ZLR 2019, 325-330 und
Stellungnahme zu den Auswirkungen des EuGH-Urteils in Rs. C-528/16 zu neuen Züchtungstechniken auf das Lebensmittelrecht
https://www.lebensmittelverband.de/de/verband/positionen/20190613-auswirkungen-eugh-urteil-zuechtungstechniken

Glas G.& Carmeliet T. (2018): **The European Court to rule on milestone in European GMO legislation: the legal classification of mutagenesis in plant breeding**. BIO-SCIENCE LAW REVIEW 16 (2), 91-104
http://www.allenovery.com/SiteCollectionDocuments/16.2%20ARTICLE%203%20(final).pdf

Gleim S., Smyth S.J. (2018): **Scientific underpinnings of biotechnology regulatory frameworks**. New Biotechnol 42, 26–32

Gleim S., Lubieniechi S., Smyth S.J. (2020): **CRISPR-Cas9 Application in Canadian Public and Private Plant Breeding.** CRISPR J. 3 (1), 44-51. doi: 10.1089/crispr.2019.0061.
Plant-breeding technologies have expanded, accelerating breeding research beyond the confines of current regulations. The application of genome editing, such as CRISPR-Cas9, do not neatly fit into existing regulatory frameworks, creating uncertainty as to whether they can be regarded as conventionally developed varieties without further regulation. This research presents the current views of Canadian plant breeders based on a national survey of plant breeders. There is evidence that a review of existing regulations is required, as >60% anticipate the use of genome-editing technologies in the next few years. This paper reviews plant-breeding practices under the context of present plants with novel trait (PNT) regulations and where plant breeders place the use of CRISPR-Cas9 within the suite of available genome-editing options. This paper establishes when and why, or why not, breeders choose to introduce CRISPR-Cas9 into their research over other plant-breeding applications.

GLP: **Human and Agriculture Gene Editing**: Regulations and Index
https://crispr-gene-editing-regs-tracker.geneticliteracyproject.org/

Gocht A., Consmüller N., Thom F., Grethe H. (2021): **Economic and Environmental Consequences of the ECJ Genome Editing Judgment in Agriculture**. *Agronomy 11* (6), 1212 | https://doi.org/10.3390/agronomy11061212
Genome-edited crops are on the verge of being placed on the market and their agricultural and food products will thus be internationally traded soon. National regulations, however, diverge regarding the classification of genome-edited crops. Major countries such as the US and Brazil do not specifically regulate genome-edited crops, while in the European Union, they fall under GMO legislation, according to the European Court of Justice (ECJ). As it is in some cases impossible to analytically distinguish between products from genome-edited plants and those from non-genome-edited plants, EU importers may fear the risk of violating EU legislation. They may choose not to import any agricultural and food products based on crops for which genome-edited varieties are available. Therefore, crop products of which the EU is currently a net importer would become more expensive in the EU, and production would intensify. Furthermore, an intense substitution of products covered and not covered by genome editing would occur in consumption, production, and trade. We analyzed the effects of such a cease of EU imports for cereals and soy in the EU agricultural sector with the comparative static agricultural sector equilibrium model CAPRI. Our results indicate dramatic effects on agricultural and food prices as well as on farm income. The intensification of EU agriculture may result in negative net environmental effects in the EU as well as in an increase in global greenhouse gas (GHG) emissions. This suggests that trade effects should be considered when developing domestic regulation for genome-edited crops.
https://www.mdpi.com/2073-4395/11/6/1212

Gocht A., Consmüller N., Thom F., Grethe H. (2020): **Economic and Environmental Consequences of the ECJ Genome Editing Judgement in Agriculture.** Thünen Working Paper 150
https://www.thuenen.de/media/publikationen/thuenen-workingpaper/ThuenenWorkingPaper_150.pdf

Grohmann L., Keilwagen J., Duensing N., Dagand E., Hartung F., Wilhelm R., Bendiek J. and Sprink T (2019): **Detection and Identification of Genome Editing in Plants: Challenges and Opportunities.** Front. Plant Sci. 10:236. | doi: 10.3389/fpls.2019.00236
Conventional genetic engineering techniques generate modifications in the genome *via* stable integration of DNA elements which do not occur naturally in this combination. Therefore, the resulting organisms and (most) products thereof can unambiguously be identified with event-specific PCR-based methods targeting the insertion site. New breeding techniques such as genome editing diversify the toolbox to generate genetic variability in plants. Several of these techniques can introduce single nucleotide changes without integrating foreign DNA and thereby generate organisms with intended phenotypes. Consequently, such organisms and products thereof might be indistinguishable from naturally occurring or conventionally bred counterparts with established analytical tools. The modifications can entirely resemble random mutations regardless of being spontaneous or induced chemically or *via* irradiation. Therefore, if an identification of these organisms or products thereof is demanded, a new challenge will arise for (official) seed, food, and feed testing laboratories and enforcement institutions. For detailed consideration, we distinguish between the *detection of sequence alterations* – regardless of their origin – the *identification of the process* that generated a specific modification and the *identification of a genotype*, i.e., an organism produced by genome editing carrying a specific genetic alteration in a known background. This article briefly reviews the existing and upcoming detection and identification strategies (including the use of bioinformatics and statistical approaches) in particular for plants developed with genome editing techniques.
https://www.frontiersin.org/articles/10.3389/fpls.2019.00236/full

Grossman M.R. (2020): **The SECURE Rule: New Regulations for Crop Biotechnology in the United States.** EFFL 6, 548-562.
In May 2020, the US Department of Agriculture enacted new regulations to govern genetically engineered organisms. The 2020 Rule focuses on the products of biotechnology and is designed to accommodate future innovation. The Rule defines genetic engineering broadly, but establishes exemptions from regulation, including certain organisms developed with innovative plant breeding techniques such as genome editing. It allows developers to determine that their new organisms are exempt, with a voluntary USDA process to confirm the exemption. A new Regulatory Status Review uses scientific risk assessment to determine whether an organism poses a plausible plant pest risk and is therefore subject to regulation. Organisms that pose plant pest risks, products intended for pharmaceutical or industrial use, and certain other GE organisms require permits for interstate movement, import, or release into the environment. The 2020 Rule reduces the regulatory burden for developers whose organisms are unlikely to pose a plant pest risk and reserves stricter USDA oversight for organisms that pose risk. Criticisms of the 2020 Rule focus on exemptions and self determinationand on the possible impact of the Rule on trade.
https://effl.lexxion.eu/article/EFFL/2020/6/5

Hamburger D.J.S. (2018): **Normative Criteria and Their Inclusion in a Regulatory Framework for New Plant Varieties Derived From Genome Editing Front.** Bioeng. Biotechnol., 19 December 2018 | https://doi.org/10.3389/fbioe.2018.00176
Any legal regulation has to take into account fundamental interests and concerns, whether of private or public nature. This applies in particular to the politically and socially sensitive question of regulating plant biotechnology. With the advent of new breeding techniques, such as genome editing, new challenges are arising for legislators around the world. However, in coping with them not only the technical particularities of the new breeding techniques must be taken into account but also the diverse and sometimes conflicting interests of the various stakeholders. In order to be able to draft a suitable regulatory regime for these new techniques, the different interests and concerns at play are identified. Subsequently, a determination is made on how these interests relate to each other, before regulatory concepts to reconcile the conflicting demands are presented. The examined normative criteria, which can have an impact on regulatory decisions regarding genome edited plants and products derived from them, include: industry interests, farmer interests, public opinion, consumer rights and interests, human health and food safety, food security, environmental protection, consistency, and coherence of the regulatory framework and ethical or religious convictions. Since those interests differ from country to country depending on the respective political, economic, and social circumstances, the respective legislator has the task of identifying these normative criteria and must find a suitable balance between them. To this end, a concept is developed on how the different interests can be related to each other and how to deal with conflicting and irreconcilable demands. Additionally, a legislator may have recourse to a number of further analyzed regulatory measures. An approval or notification procedure can be used for a risk assessment or a socio-economic evaluation. Coexistence measures and labeling provisions are able to reconcile interests that are at odds with each other and the precautionary principle can justify certain safeguard measures. As a result, the individual country-specific regulatory outcomes regarding genome edited plants are likely to be as manifold as the interests and regulatory measures at hand.
https://www.frontiersin.org/articles/10.3389/fbioe.2018.00176/full

Harfouche A.L., Petousi V., Meilan R., Sweet J. Twardowski T., Altman A. (2021**): Promoting Ethically Responsible Use of Agricultural Biotechnology.** Trends in Plant Science | https://doi.org/10.1016/j.tplants.2020.12.015
Growing global demands for food, bioenergy, and specialty products, along with the threat posed by various environmental changes, present substantial challenges for agricultural production. Agricultural biotechnology offers a promising avenue for meeting these challenges; however, ethical and sociocultural concerns must first

be addressed, to ensure widespread public trust and uptake. To be effective, we need to develop solutions that are ethically responsible, socially responsive, relevant to people of different cultural and social backgrounds, and conveyed to the public in a convincing and straightforward manner. Here, we highlight how ethical approaches, principled decision-making strategies, citizen stakeholder participation, effective science communication, and bioethics education should be used to guide responsible use of agricultural biotechnology.
https://www.cell.com/trends/plant-science/fulltext/S1360-1385(20)30392-7 pdf-file available

Hartung U. (2020): **Inside Lobbying on the Regulation of New Plant Breeding Techniques in the European Union: Determinants of Venue Choices.** Review of Policy Research, (2020) 10.1111/ropr.12366 | https://doi.org/10.1111/ropr.12366
In July 2018, the Court of Justice of the European Union decided that new plant breeding techniques (NPBTs) fall within the scope of the restrictive provisions on genetically modified organisms (GMOs). Previously, various actors had lobbied in order to influence the European Union's (EU's) regulatory decision on NPBTs. This study examines the venue choices taken by Cibus, a biotech company that promoted NPBT deregulation. It shows that the firm bypassed the EU level and that it lobbied competent authorities (CAs) in certain member states to gain support for the deregulation of NPBTs. Cibus chose the CAs because their institutional "closedness" reduced the risk of the debate over the deregulation of NPBTs becoming public. However, the CA's specific competences and their influence on EU decision making were of likewise importance. The firm lobbied CAs based in Finland, Germany, Ireland, Sweden, Spain, and the United Kingdom. Two factors appear to have influenced Cibus' choices for these countries: high-level political support for agribiotech and the high relevance of biotech sectors. In contrast, public support for GMOs turned out to have hardly any influence, and virtually no association could be observed for the agricultural application of biotechnology in the past nor for the weakness of domestic anti-GMO lobby groups. Finally, the in-depth study on Germany affirms that "closedness" was important for Cibus' choices and reveals that technical information served as a venue-internal factor that influenced the firm's choices.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/ropr.12366

Hill N. (2020): **Public Opinion of Gene-Editing in Agriculture: A Mixed-Method Study of Online Media and Metaphors**
https://ttu-ir.tdl.org/bitstream/handle/2346/86569/HILL-DISSERTATION-2020.pdf?sequence=1&fbclid=IwAR1_2R4OFrtCdCHdAhMsFp3b975Od9xL7tqpXHqNBOXhfmFgyLOVbQXTGLs

Huang, X., Hilscher, J., Stoger, E. et al. (2021): **Modification of cereal plant architecture by genome editing to improve yields.** Plant Cell Rep | https://doi.org/10.1007/s00299-021-02668-7
Plant architecture is defined as the three-dimensional organization of the entire plant. Shoot architecture refers to the structure and organization of the aboveground components of a plant, reflecting the developmental patterning of stems, branches, leaves and inflorescences/flowers. Root system architecture is essentially determined by four major shape parameters—growth, branching, surface area and angle. Interest in plant architecture has arisen from the profound impact of many architectural traits on agronomic performance, and the genetic and hormonal regulation of these traits which makes them sensitive to both selective breeding and agronomic practices. This is particularly important in staple crops, and a large body of literature has, therefore, accumulated on the control of architectural phenotypes in cereals, particularly rice due to its twin role as one of the world's most important food crops as well as a model organism in plant biology and biotechnology. These studies have revealed many of the molecular mechanisms involved in the regulation of tiller/axillary branching, stem height, leaf and flower development, root architecture and the grain characteristics that ultimately help to determine yield. The advent of genome editing has made it possible, for the first time, to introduce precise mutations into cereal crops to optimize their architecture and close in on the concept of the ideotype. In this review, we consider recent genome editing studies that have focused on the examination (or reexamination) of plant architectural phenotypes in cereals and the modification of these traits for crop
https://link.springer.com/article/10.1007/s00299-021-02668-7

Huang, T.K., Puchta, H. (2021): **Novel CRISPR/Cas applications in plants: from prime editing to chromosome engineering.** Transgenic Res **|** https://doi.org/10.1007/s11248-021-00238-x
In the last years, tremendous progress has been made in the development of CRISPR/Cas-mediated genome editing tools. A number of natural CRISPR/Cas nuclease variants have been characterized. Engineered Cas proteins have been developed to minimize PAM restrictions, off-side effects and temperature sensitivity. Both kinds of enzymes have, by now, been applied widely and efficiently in many plant species to generate either single or multiple mutations at the desired loci by multiplexing. In addition to DSB-induced mutagenesis, specifically designed CRISPR/Cas systems allow more precise gene editing, resulting not only in random mutations but also in predefined changes. Applications in plants include gene targeting by homologous recombination, base editing and, more recently, prime editing. We will evaluate these different technologies for their prospects and practical applicability in plants. In addition, we will discuss a novel application of the Cas9 nuclease in plants, enabling the induction of heritable chromosomal rearrangements, such as inversions and translocations. This technique will make it possible to change genetic linkages in a programmed way and add another level of genome engineering to the toolbox of plant breeding. Also, strategies for tissue culture free genome editing were developed, which might be helpful to overcome the transformation bottlenecks in many crops. All in all, the recent advances of CRISPR/Cas technology will help agriculture to address the challenges of the twenty-first century related to global warming, pollution and the resulting food shortage.

https://link.springer.com/article/10.1007/s11248-021-00238-x

Hundleby P.A.C. & Harwood W.A. (2018): **Impacts of the EU GMO regulatory framework for plant genome editing.** *Food Energy Secur.* ; e00161. | https://doi.org/10.1002/fes3.161
New plant breeding technologies, such as genome editing, are enabling new crop varieties to be developed far quicker and with greater precision and scope than achievable using conventional methods. These advances could help farmers address the challenges of climate change, sustainability, and global food security. However, despite their potential, the uptake of these new technologies has been slowed down due to the uncertainty associated with the regulation of genome edited crops. For many European consumers, their view of new breeding technologies is influenced by many factors. Those who have never faced a major food crisis may not sufficiently appreciate the challenges posed by a projected rise of 2 billion in the human population by 2050. In addition, consumers with a regular and plentiful supply of food may not have to consider how their food is produced, or appreciate the challenges EU farmers are already facing to meet future demand. Misleading online articles, questioning the safety and ethics of these "new" biotech foods, can also lead consumers to be reluctant to accept them. Consequently, Europe's mixed view on biotech crops may also be hindering their adoption in countries who have even more to gain from the technology. In this review, we discuss the current data on global and EU GM crop adoption and the potential impact a new wave of crop development may have for agriculture. We reflect on how the EU has viewed GM crops, and we consider the future of both genetic modification (GM) and genome editing (GE) in the EU. We explore lessons learnt from the adoption of GM crops and examine the potential impact the recent decision not to exempt genome edited crops from the EU GMO Directive, will have on EU farmers, scientists, consumers, trading countries, and the rest of the world.
https://onlinelibrary.wiley.com/doi/full/10.1002/fes3.161 guter Vergleich EU und Welt

High Level Group of Scientific Advisors / Scientific Advice Mechanism (SAM):
A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive, November 2018
https://op.europa.eu/en/publication-detail/-/publication/a9100d3c-4930-11e9-a8ed-01aa75ed71a1/language-en/format-PDF/source-94584603

Hillary V. E., Ceasar S.A. (2019): **Application of CRISPR/Cas9 Genome Editing System in Cereal Crops.** The Open Biotechnology Journal 13, 173-179 | 10.2174/1874070701913010173
Recent developments in targeted genome editing accelerated genetic research and opened new potentials to improve the crops for better yields and quality. Genome editing techniques like Zinc Finger Nucleases (ZFN) and Transcription Activator-Like Effector Nucleases (TALENs) have been accustomed to target any gene of interest. However, these systems have some drawbacks as they are very expensive and time consuming with labor-intensive protein construction protocol. A new era of genome editing technology has a user-friendly tool which is termed as Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-CRISPR associated protein9 (Cas9), is an RNA based genome editing system involving a simple and cost-effective design of constructs. CRISPR/Cas9 system has been successfully applied in diverse crops for various genome editing approaches. In this review, we highlight the application of the CRISPR/Cas9 system in cereal crops including rice, wheat, maize, and sorghum to improve these crops for better yield and quality. Since cereal crops supply a major source of food to world populations, their improvement using recent genome editing tools like CRISPR/Cas9 is timely and crucial. The genome editing of cereal crops using the CRISPR/Cas9 system would help to overcome the adverse effects of agriculture and may aid in conserving food security in developing countries.
https://openbiotechnologyjournal.com/contents/volumes/V13/TOBIOTJ-13-173/TOBIOTJ-13-173.pdf

Holme I.B., Gregersen P.L. and Brinch-Pedersen H. (2019): **Induced Genetic Variation in Crop Plants by Random or Targeted Mutagenesis: Convergence and Differences.** Front. Plant Sci. | https://doi.org/10.3389/fpls.2019.01468
New Breeding Techniques (NBTs) include several new technologies for introduction of new variation into crop plants for plant breeding, in particular the methods that aim to make targeted mutagenesis at specific sites in the plant genome (NBT mutagenesis). However, following that the French highest legislative body for administrative justice, the Conseil d'État, has sought advice from The Court of Justice of the European Union (CJEU) in interpreting the scope of the genetically modified organisms (GMO) Directive, CJEU in a decision from 2018, stated that organisms modified by these new techniques are not exempted from the current EU GMO legislation. The decision was based in a context of conventional plant breeding using mutagenesis of crop plants by physical or chemical treatments. These plants are explicitly exempted from the EU GMO legislation, based on the long-termed use of mutagenesis. Following its decision, the EU Court considers that the NBTs operate "at a rate out of all proportion to those resulting from the application of conventional methods of mutagenesis." In this paper, we argue that in fact this is not the case anymore; instead, a convergence has taken place between conventional mutagenesis and NBTs, in particular due to the possibilities of TILLING methods that allow the fast detection of mutations in any gene of a genome. Thus, by both strategies mutations in any gene across the genome can be obtained at a rather high speed. However, the differences between the strategies are 1) the precision of the exact site of mutation in a target gene, and 2) the number of off-target mutations affecting other genes than the target gene. Both aspects favour the NBT methods, which provide more precision and fewer off-target mutations. This is in stark contrast to the different status of the two technologies with respect to EU GMO legislation. In the

future, this situation is not sustainable for the European plant breeding industry, since it is expected that restrictions on the use of NBTs will be weaker outside Europe. This calls for reconsiderations of the EU legislation of plants generated *via* NBT mutagenesis
https://www.frontiersin.org/articles/10.3389/fpls.2019.01468/full

Hucho F., Diekämper J., Fangerau H., Fehse B., Hampel J., Köchy K., Könninger S., Marx-Stölting L., Müller-Röber B., Reich J., Schickl H., Taupitz J., Walter J., Zenke M., Korte M. (Sprecher) (Hrsg.): **Vierter Gentechnologiebericht. Bilanzierung einer Hochtechnologie.** Baden-Baden: Nomos. 1. Auflage 2018. ISBN print: 978-3-8487-5183-9, ISBN online: 978-3-8452-9379-0, DOI: 10.5771/9783845293790.
https://www.nomos-elibrary.de/10.5771/9783845293790/vierter-gentechnologiebericht.
Eine Kurzfassung des Berichts hier: http://www.gentechnologiebericht.de/bilder/BBAW_Broschure-Inhalt_IV-Gentechnologiebericht_PDFA-1b.pdf

Ishii T. (2018): **Crop Gene-Editing: Should We Bypass or Apply Existing GMO Policy? Trends in Biotechnology:** https://doi.org/10.1016/j.tplants.2018.09.001
Recent advances in crop gene-editing technologies allow for efficient site-specific mutagenesis without introducing exogenous DNA, potentially bypassing product-based genetically modified organism (GMO) regulations. Conversely, such plants can be subject to process-based GMO regulations. However, it is important to tailor existing GMO regulations with the aim to ensure social acceptance of gene-edited crops.
https://www.sciencedirect.com/science/article/pii/S1360138518301936

Ishii T. (2019) **Regulation of Genome Editing in Plant Biotechnology: Japan.** In: Dederer HG., Hamburger D. (eds) Regulation of Genome Editing in Plant Biotechnology. Springer, Cham
To regulate the research and industrial uses of genetically modified organisms (GMOs), Japan enacted the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms 2003. This law can be regarded as a product-based GMO regulation. To date, Japan has approved 133 GM crop varieties for cultivation, distribution, and import, thus becoming a major importer of GM crops in the world. However, no GM crops have been commercially cultivated in Japan, except one ornamental GM flower. A recent consumer survey showed that 40.7% of respondents expressed concern over the safety of GM food products. Meanwhile, some Japanese researchers have already used robust genome editing techniques, such as CRISPR-Cas9, and reported gene-disrupted apple, potato, soybean, tomato and rice. In 2017, a GM rice variety was approved as Japan's first field trial of a genome edited crop. In contrast, some citizen groups expressed opposition to the cultivation test and demanded the regulation of genome edited crops. However, relevant ministries have not considered the regulation of any uses of genome editing in earnest. The current state of Japan does not warrant a promising future of genome edited crops.
https://link.springer.com/chapter/10.1007/978-3-030-17119-3_6

Itoh, T., Onuki, R., Tsuda, M. et al. (2020): **Foreign DNA detection by high-throughput sequencing to regulate genome-edited agricultural products.** Sci Rep 10**,** 4914 |
https://doi.org/10.1038/s41598-020-61949-5
Although the advent of several new breeding techniques (NBTs) is revolutionizing agricultural production processes, technical information necessary for their regulation is yet to be provided. Here, we show that high-throughput DNA sequencing is effective for the detection of unintended remaining foreign DNA segments in genome-edited rice. A simple *k*-mer detection method is presented and validated through a series of computer simulations and real data analyses. The data show that a short foreign DNA segment of 20 nucleotides can be detected and the probability that the segment is overlooked is 10^{-3} or less if the average sequencing depth is 30 or more, while the number of false hits is less than 1 on average. This method was applied to real sequencing data, and the presence and absence of an external DNA segment were successfully proven. Additionally, our in-depth analyses also identified some weaknesses in current DNA sequencing technologies. Hence, for a rigorous safety assessment, the combination of *k*-mer detection and another method, such as Southern blot assay, is recommended. The results presented in this study will lay the foundation for the regulation of NBT products, where foreign DNA is utilized during their generation.
https://www.nature.com/articles/s41598-020-61949-5.pdf

Janik E., Niemcewicz M., Ceremuga M., Krzowski L., Saluk-Bijak J., Bijak M. (2020): **Various Aspects of a Gene Editing System—CRISPR–Cas9***. Int. J. Mol. Sci. 21*(24), 9604; |
https://doi.org/10.3390/ijms21249604
The discovery of clustered, regularly interspaced short palindromic repeats (CRISPR) and their cooperation with CRISPR-associated (Cas) genes is one of the greatest advances of the century and has marked their application as a powerful genome engineering tool. The CRISPR–Cas system was discovered as a part of the adaptive immune system in bacteria and archaea to defend from plasmids and phages. CRISPR has been found to be an advanced alternative to zinc-finger nucleases (ZFN) and transcription activator-like effector nucleases (TALEN) for gene editing and regulation, as the CRISPR–Cas9 protein remains the same for various gene targets and just a short guide RNA sequence needs to be altered to redirect the site-specific cleavage. Due to its high efficiency and precision, the Cas9 protein derived from the type II CRISPR system has been found to have applications in many fields of science. Although CRISPR–Cas9 allows easy genome editing and has a number of benefits, we

should not ignore the important ethical and biosafety issues. Moreover, any tool that has great potential and offers significant capabilities carries a level of risk of being used for non-legal purposes. In this review, we present a brief history and mechanism of the CRISPR–Cas9 system. We also describe on the applications of this technology in gene regulation and genome editing; the treatment of cancer and other diseases; and limitations and concerns of the use of CRISPR–Cas9
https://www.mdpi.com/1422-0067/21/24/9604

Jany Kl.-D. (2019): **Änderungsbedarf beim Gentechnikgesetz.** Editorial: BIUZ 5/2019

Jany Kl.-D. (2018): **Das EuGH-Urteil und die Folgen für die Grüne, Weiße und Rote Biotechnologie-** transkript 10

Jany Kl.-D. – Interview (2018): **„Ein neues Gesetz tut not“** transkript 11-12

Jany, Freyssinet, Dumont: **Enabling genome editing to make Europe's agriculture more sustainable**
https://www.europeanscientist.com/en/features/enabling-genome-editing-to-make-europes-agriculture-more-sustainable/

Jiang L. (2020): **Commercialization of the gene-edited crop and morality: challenges from the liberal patent law and the strict GMO law in the EU**, New Genetics and Society, 39:2, 191-218, DOI: 10.1080/14636778.2019.1686968
The EU aspires to utilize the economic advantages of gene-editing technology on one hand and ensure human health and environmental safety on the other. Surrounding the fierce debates over emerging gene-edited plant, the current debate focused on the issue of whether the gene-edited crop should be within or outside the GMO law and its implication for innovation. It should not be forgotten that it is also involved in the complex patentability issues pertaining to the legal interpretation of the patent law. The gene-edited crop is governed by GMO regulations due to its potential risk to human health and environmental safety. But it is heavily patented, as patent regulations ignore its potential risk. This article examines the discrepancy of the gene-edited crop between the existing GMO law and the patent law and reveals the challenges to current EU jurisdiction, including the international trade impediment challenge, the patent monopoly challenge, the market confusion challenge, and the agricultural economy suspension challenge. In the end, this article argues that EU GMO regulations should be bridged with a patent system in facing the regulatory challenges from the gene-edited crop.
https://www.tandfonline.com/doi/abs/10.1080/14636778.2019.1686968

Jorasch, P. **Will the EU stay out of step with science and the rest of the world on plant breeding innovation?**. Plant Cell Rep 39**,** 163–167 (2020). https://doi.org/10.1007/s00299-019-02482-2
Innovations in plant breeding like genome editing methods raised questions about the adequacy of established regulatory policies for plant breeding and biotechnology in view of these new breeding methods and the resulting products. Most countries follow the principle approach that only those plants will be regulated under biotech regulations that include a novel combination of genetic material following the Cartagena protocol. In contrast to this, the European Court of Justice interpreted the current EU biotech regulations in a way that these also apply to plants resulting from new mutagenesis breeding, even if these plants are indistinguishable from conventionally bred plants. This ruling created strong reactions and concerns stating that recent technical developments have made the EU GMO Directive no longer fit for purpose. The article describes ongoing policy developments on EU level that might result in an update of current regulations.
https://link.springer.com/article/10.1007/s00299-019-02482-2

Jorasch P. (2019): **The global need for plant breeding Innovation**. Transgenic. Res. 28, 81-86 | https://doi.org/10.1007/s11248-019-00138-1
Representing National Seed Associations and Companies in 75 countries, the International Seed Federation (ISF) is the voice of the global seed sector and stands for a world where the best quality seed is accessible to all, supporting sustainable agriculture and food security. ISF's mission is to create the best environment for the global movement of seed and to promote plant breeding and innovation. In view to meet the global challenges like climate change, a growing world population and the need for resource efficient farming systems, plant breeding innovation will definitely need to play a role (Fig. 1). New plant varieties that can better stand pests and diseases with fewer inputs, plants that have stabile yield despite a changing climate and plants with increased productivity, by maximizing resource use efficiency in regard of water, land and nutrients can contribute to meet these goals (Pereira 2016).
https://link.springer.com/content/pdf/10.1007%2Fs11248-019-00138-1.pdf

JRC F7 - Knowledge Health and Consumer Safety, **Overview of EU National Legislation on Genomics**, JRC Science for Policy Report, Luxembourg: European Commission, EUR 29404 EN, ISBN 978-92-79-96740-5, doi:10.2760/04463, PUBSY No. JRC113479

With the advent of fast, high efficiency and low cost DNA sequencing techniques, the ability to study the human genome by reading the sequence of its DNA is growing exponentially, with a resulting tremendous impact on many fields of scientific research. The application of genomics inside routine healthcare is boosting preventive medicine practices and can lead to personalised treatments that can highly improve the healthcare services and patients' health, and in the same time provide a wealth of data for medical research. In parallel, this has also led to the spread of commercial opportunities to provide consumers with the possibility of sequencing their genomes in a way which is both appealing and affordable. These commercial offers, however, do not always ensure the security of the generated data. In addition, the accuracy and reliability of the offered findings are not homogenous, as there are no standards to guarantee that the quality of the outputs satisfies minimum requirements - in fact, no agreements yet exist on the definition of these requirements. In this frame, a comprehensive knowledge of what is present at the legislative level in the member states of the European Union (plus Switzerland, Iceland and Norway) regarding the regulatory oversight of genomics technologies is of fundamental importance to frame the status of existing European norms, to understand whether possible incompatibilities might arise between frameworks and to highlight eventual gaps.
http://publications.jrc.ec.europa.eu/repository/bitstream/JRC113479/policy_report_-_review_of_eu_national_legislation_on_genomics_-_with_identifiers.pdf

Kahrmann J. and Leggewie G. (2018): **CJEU's Ruling Makes Europe's GMO Legislation Ripe for Reformation.** Zeitschrift für Europäisches Umwelt- und Planungsrecht 16 (4), 497 - 504
Am 25.7.2018 urteilte der EuGH, dass alle Organismen, die mit Genome Editing Techniken hergestellt wurden, in den Anwendungsbereich des europäischen Gentechnikrechts fallen. Fast so kritikwürdig wie die sehr streitbaren wissenschaftlichen Grundaussagen, auf denen das Urteil fußt, ist die unterlassene eingehende Begründung der Entscheidung. Spätestens nach diesem Urteil ist das europäische Gentechnikrecht nicht zukunftsfähig. Dies verlangt nach einem gesetzgeberischen Handeln auf EU-Ebene.
https://eurup.lexxion.eu/article/EURUP/2018/4/10?_locale=en

Karagyaur M.N., Efimenko A.Y., Makarevich P.I., Vasiluev P.A., Akopyan Z.A., Bryzgalina E.V. Tkachuk V.A, (2019): **Ethical and Legal Aspects of Using Genome Editing Technologies in Medicine (Review).**
According to many experts, the turning point in the development of genome editing technologies (GET) was 2012, when Feng Zhang and Jennifer Doudna independently proposed the adaptive bacterial immunity system CRISPR/Cas9 for editing the genome of living cells of eukaryotic organisms. Since then, the range of applications of CRISPR/Cas9 technology and related GET has continued to grow like an avalanche. Thus, new genetically modified microorganisms, plants, and animals have been created, the experimental studies on the genetic foundations of life have greatly expanded, and revolutionary approaches to therapy and prevention of incurable diseases have been developed. However, the indisputable advantages of GET are associated with high risks (real and potential) to the environment, human health, and society as a whole. Significant progress in the genome editing in eukaryotes has led to a rapid appearance of humans with an "improved" genome, despite the openly expressed opposition of leading scientists working in this field. Among them, David Baltimore, Paul Berg, Jennifer Doudna, George Church, and Martin Jinek are calling for a global suspension of work with human embryos until the technical, legal and ethical standards in this area are developed. There is an urgent need for the development of an unambiguous public position and improvement of the regulatory framework for the GET, including that in the Russian Federation; the present review attempts to address the urgent issue of GET-related regulations. We discuss various approaches to regulating the use of GET in medicine. We review legal acts and ethical recommendations around the world concerning the GET-mediated modification of the plant and animal genetic material for the purpose of creating medical products and drugs. We also address the sensitive issue of editing the genome of human cells (somatic or germ). Special attention is paid to the relevant legal and ethical standards exiting in the Russian Federation. The presented data allow for a better understanding of the current situation and the areas of further research into GET, where the development and implementation of regulatory standards are especially urgent.
https://cyberleninka.ru/article/n/ethical-and-legal-aspects-of-using-genome-editing-technologies-in-medicine-review

Karky R.B. and Perry M. (2019): **Disharmonization in the Regulation of Transgenic Plants in Europe.** Biotechnology Law ReportVol. 38, No. 6 | https://doi.org/10.1089/blr.2019.29135.rbk
https://doi.org/10.1089/blr.2019.29135.rbk

Kawall K. (2018): Genome Editing ohne Risiko? GID 274
Neue Gentechnikverfahren, insbesondere die Techniken des Genome Editing, gelten gegenüber früheren Gentechniken als präziser. Doch auch mit ihrer Nutzung sind Risiken verbunden.

Khalil, A.M. (2020): **The genome editing revolution: review.** J Genet Eng Biotechnol 18**,** 68 | https://doi.org/10.1186/s43141-020-00078-y
Background: Development of efficient strategies has always been one of the great perspectives for biotechnologists. During the last decade, genome editing of different organisms has been a fast advancing field and therefore has received a lot of attention from various researchers comprehensively reviewing latest achievements and offering opinions on future directions. This review presents a brief history, basic principles, advantages and

disadvantages, as well as various aspects of each genome editing technology including the modes, applications, and challenges that face delivery of gene editing components.
Main body:Genetic modification techniques cover a wide range of studies, including the generation of transgenic animals, functional analysis of genes, model development for diseases, or drug development. The delivery of certain proteins such as monoclonal antibodies, enzymes, and growth hormones has been suffering from several obstacles because of their large size. These difficulties encouraged scientists to explore alternative approaches, leading to the progress in gene editing. The distinguished efforts and enormous experimentation have now been able to introduce methodologies that can change the genetic constitution of the living cell. The genome editing strategies have evolved during the last three decades, and nowadays, four types of "programmable" nucleases are available in this field: meganucleases, zinc finger nucleases, transcription activator-like effector nucleases, and the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR associated protein 9 (Cas9) (CRISPR/Cas-9) system. Each group has its own characteristics necessary for researchers to select the most suitable method for gene editing tool for a range of applications. Genome engineering/editing technology will revolutionize the creation of precisely manipulated genomes of cells or organisms in order to modify a specific characteristic. Of the potential applications are those in human health and agriculture. Introducing constructs into target cells or organisms is the key step in genome engineering.
Conclusions: Despite the success already achieved, the genome editing techniques are still suffering certain difficulties. Challenges must be overcome before the full potential of genome editing can be realized.
https://jgeb.springeropen.com/articles/10.1186/s43141-020-00078-y

Kaul, T., Sony, S.K., Verma, R. et al. (2020): **Revisiting CRISPR/Cas-mediated crop improvement: Special focus on nutrition.** J Biosci 45**,** 137 (2020). https://doi.org/10.1007/s12038-020-00094-7
Genome editing (GE) technology has emerged as a multifaceted strategy that instantaneously popularised the mechanism to modify the genetic constitution of an organism. The clustered regularly interspaced short palindromic repeat (CRISPR) and CRISPR-associated (Cas) protein-based genome editing (CRISPR/Cas) approach has huge potential for efficacious editing of genomes of numerous organisms. This framework has demonstrated to be more economical in contrast to mega-nucleases, zinc-finger nucleases (ZFNs), and transcription activator-like effector nucleases (TALENs) for its flexibility, versatility, and potency. The advent of sequence-specific nucleases (SSNs) allowed the precise induction of double-strand breaks (DSBs) into the genome, ensuring desired alterations through non-homologous end-joining (NHEJ) or homology-directed repair (HDR) pathways. Researchers have utilized CRISPR/Cas-mediated genome alterations across crop varieties to generate desirable characteristics for yield enhancement, enriched nutritional quality, and stress-resistance. Here, we highlighted the recent progress in the area of nutritional improvement of crops via the CRISPR/Cas-based tools for fundamental plant research and crop genetic advancements. Application of this genome editing aids in unraveling the basic biology facts in plants supplemented by the incorporation of genome-wide association studies, artificial intelligence, and various bioinformatic frameworks, thereby providing futuristic model studies and their affirmations. Strategies for reducing the 'off-target' effects and the societal approval of genome-modified crops developed via this modern biotechnological approach have been reviewed.
https://link.springer.com/article/10.1007/s12038-020-00094-7

Kearns, P. (2019). **An overview of OECD activities related to modern techniques of biotechnology and genome editing.** Transgenic Res 28 (Suppl 2): 41. |
https://doi.org/10.1007/s11248-019-00131-8
https://link.springer.com/content/pdf/10.1007%2Fs11248-019-00131-8.pdf

Kleter G.A., Kuiper H-A., Kok E.J. (2019): **Gene-Edited Crops: Towards a Harmonized Safety Assessment.** Trends in Biotechnology 37 (5), 443-447
https://doi.org/10.1016/j.tibtech.2018.11.014
Gene editing and other innovative plant breeding techniques are transforming the field of crop biotechnology. Divergent national regulatory regimes worldwide apply to crops bred with these techniques. A plea is made for international harmonization of the premarket assessment of their safety. Such harmonization has previously been achieved for genetically modified (GM) crops.
https://www.sciencedirect.com/science/article/pii/S0167779918303378?dgcid=author

Kok E.J., Glandorf D. C.M., Prins T.W., Visser R.G.F. (2019): **Food and environmental safety assessment of new plant varieties after the European Court decision: process-triggered or product-based?** Trends in Food Science & Technology |.
https://doi.org/10.1016/j.tifs.2019.03.007
Background: For the safety assessment of new plant varieties most countries have adopted a basically process-triggered legislation where the techniques applied in the plant breeding strategy determine the procedure for market approval. In other countries, there is a more product-based legislation where the characteristics of new plant varieties determine the procedure for market approval.
Scope and Approach: In the present paper it is investigated whether the knowledge on current plant breeding strategies warrants the current distinction in safety assessment between the different types of techniques applied. Related to this it is assessed whether it is feasible to enforce any future legislation of plants obtained by new plant breeding techniques, based on traceability aspects related to the different gene editing strategies.

Key Findings and Conclusions: It is concluded that unintended side effects can be related to any of the current plant breeding techniques, but the effects and associated frequencies of the mutations cannot be predicted and insufficient data are available to relate them to specific techniques. As a consequence, there is no scientific basis to state that the breeding technique applied should determine the nature and extent of the pre-market safety assessment of any new plant variety. Furthermore, it will not be feasible to analytically distinguish many of the varieties obtained by new plant breeding techniques from conventionally bred varieties. This study shows that only a truly product-based approach, assessing each new plant variety on its own merits in terms of altered characteristics and related hazards, will guarantee the safety of our food supply as well as the environmental safety.
https://www.sciencedirect.com/science/article/abs/pii/S0924224418306630

Keiper F. and Atanassova A. (2020): **Regulation of Synthetic Biology: Developments Under the Convention on Biological Diversity and Its Protocols**. Front. Bioeng. Biotechnol. | https://doi.org/10.3389/fbioe.2020.00310
The primary international forum deliberating the regulation of "synthetic biology" is the Convention on Biological Diversity (CBD), along with its subsidiary agreements concerned with the biosafety of living modified organisms (LMOs; Cartagena Protocol on Biosafety to the CBD), and access and benefit sharing in relation to genetic resources (Nagoya Protocol to the CBD). This discussion has been underway for almost 10 years under the CBD agenda items of "synthetic biology" and "new and emerging issues relating to the conservation and sustainable use of biological diversity," and more recently within the scope of Cartagena Protocol topics including risk assessment and risk management, and "digital sequence information" jointly with the Nagoya Protocol. There is no internationally accepted definition of "synthetic biology," with it used as an umbrella term in this forum to capture "new" biotechnologies and "new" applications of established biotechnologies, whether actual or conceptual. The CBD debates are characterized by polarized views on the adequacy of existing regulatory mechanisms for "new" types of LMOs, including the scope of the current regulatory frameworks, and procedures and tools for risk assessment and risk mitigation and/or management. This paper provides an overview of international developments in biotechnology regulation, including the application of the Cartagena Protocol and relevant policy developments, and reviews the development of the synthetic biology debate under the CBD and its Protocols, including the major issues expected in the lead up to and during the 2020 Biodiversity Conference.
https://www.frontiersin.org/articles/10.3389/fbioe.2020.00310/full?&utm_source=Email_to_authors_&utm_medium=Email&utm_content=T1_11.5e1_author&utm_campaign=Email_publication&field=&journalName=Frontiers_in_Bioengineering_and_Biotechnology&id=532522

Kritikos M. (2018): **'Governing Gene Editing in the European Union: Legal and Ethical Considerations', Ethics and Integrity in Health and Life Sciences Research** (Advances in Research Ethics and Integrity, Volume 4). Emerald Publishing Limited, pp. 99-114 || https://doi.org/10.1108/S2398-601820180000004007
The chapter analyses the re-emergence of gene editing as an object of policy attention at the European Union (EU) level. Editing the genome of plants and/or animals has been a rather controversial component of all EU policies on agricultural biotechnology since the late 1980s. The chapter examines in detail the various initiatives that have been assumed for the regulation of gene editing at the EU level. Since the first political and legislative attempts, the field has been revolutionized with the development of the CRISPR-Cas9 system, which is comparatively much easier to design, produce, and use. Beyond the pure, safety-driven scientific questions, gene editing, in its contemporary form, raises a series of ethical and regulatory questions that are discussed in the context of the legal options and competences of the EU legislators. Special attention is paid to questions about the legal status of gene editing in Europe and the adequacy of the current GMO framework to deal with all the challenges associated with the latest scientific developments in the field of gene editing with a special focus on gene drive. Given the ongoing discussions regarding the ethical tenets of gene editing, the chapter investigates the question on whether there is a need to shape an EU-wide "intervention" that will address the complex and dynamic socio-ethical challenges of gene editing and puts forward a series of proposals for the framing of an inclusive framework that will be based on the need to re-enforce public trust in the EU governance of emerging technologies.
https://www.emerald.com/insight/content/doi/10.1108/S2398-601820180000004007/full/html

Kuzma J.: (2019): **Procedurally Robust Risk Assessment Framework for Novel Genetically Engineered Organisms and Gene Drives.** Regulation & Governance | doi:10.1111/rego.12245
In this article, a new framework for improving risk assessments of novel genetically engineered organisms (GEOs) is developed and applied. The Procedurally Robust Risk Assessment Framework (PRRAF) provides a set of principles and criteria for assessing and enhancing risk assessment protocols for GEOs under conditions of high uncertainty. The application of PRRAF is demonstrated using the case of a genetically engineered mosquito designed to kill its wild population and therefore decrease disease transmission. Assessments for regulatory approval of this genetically engineered insect fall short of several PPRAF criteria under the principles of humility, procedural validity, inclusion, anticipation, and reflexivity. With the emergence of GEOs designed to spread in ecosystems, such as those with gene drives, it will become increasingly important for regulatory agencies and technology developers to bolster their risk analysis methods and processes prior to field testing. PRRAF can be used as a flexible guide for doing so within a variety of institutional, regulatory, and governance contexts.
https://onlinelibrary.wiley.com/doi/full/10.1111/rego.12245

Kuzma J. and Grieger K. (2020): **Community-led governance for gene-edited crops.** Science 370 (6519), 916-918 | DOI: 10.1126/science.abd1512
In August 2020, the U.S. Department of Agriculture (USDA) began implementing new regulations for genetically engineered (GE) organisms, the SECURE (sustainable, ecological, consistent, uniform, responsible, efficient) rule (*1*). SECURE marks the first comprehensive reform of U.S. genetically modified (GM) crop oversight since the agency's initial approach in 1987 (and after several unsuccessful attempts to update its regulations over the past two decades) [see (*1*) for definitions of GE and GM crops]. The USDA estimates that under this substantial departure from its prior approach, 99% of GM plants will be exempt from premarket field testing and data-based risk assessment requirements (*2*). This rule has potential implications for international trade as the European Union (EU) is taking a more stringent approach to regulating gene-edited crops and will track them in the marketplace (*3*). We are also concerned that developers of gene-edited and GM (i.e., biotech) crops, who largely support the SECURE approach (*4*), are reconstituting the same conditions that led to public rejection and mistrust of the first generation of GM foods (*3*). To earn greater public trust and transparency, as well as enhance the ability to track gene-edited plants entering the marketplace, we therefore propose a "community-led and responsible governance" (CLEAR-GOV) coalition and certification process for biotech crop developers based on transparent information sharing about current and anticipated market uses of biotech crop varieties.
https://science.sciencemag.org/content/370/6519/916

Ladu L (2020) **The governance of genome editing techniques for the European bio-based industry,** Journal of Environmental Policy & Planning, DOI: 10.1080/1523908X.2020.1850247
Genome editing techniques (GETs) could support the transition towards a circular bio-based economy. This would require a regulatory framework that enables technical and scientific progress while ensuring safety for humans and environment. In this context, there is a debate among stakeholders in Europe whether products resulting from GETs should be subject to the GMO legislation. This paper analyses different stakeholder positions and underlying arguments on this question based on the Politically Inherent Dynamics Approach (PIDA). This takes into consideration the role of actor interests, the problem structure, institutions and alternative instruments. The analysis, based on a series of expert interviews and a Delphi survey, reveals that differing stakeholder positions are strongly shaped by differing beliefs and interests. This leads to a divergence in the definition of the problem structure, and the related solutions, in terms of the institutional set-up and alternative instruments considered. It highlights the need to reach a shared vision among actors of the problems that need to be solved, in order to understand if GETs can be considered as one potential 'solution', embracing the precautionary and innovation principles. Alternative instruments are proposed, including a call for higher stakeholder engagement and diverse regulatory instruments.
https://www.tandfonline.com/doi/abs/10.1080/1523908X.2020.1850247?journalCode=cjoe20

Lang A., Spök A., Gruber M., Harrer D., Hammer C., Winkler F., Kaelin L., Hönigmayer H., Sommer A., Wuketich M., Fuchs M., Griessler E. (2019): **Genome Editing – Interdisziplinäre Technikfolgenabschätzung.** TA-SWISS Publikationsreihe (Hrsg.): TA 70/2019. Zürich
https://www.research-collection.ethz.ch/bitstream/handle/20.500.11850/360720/9783728139825.pdf?sequence=1&isAllowed=y

Lassoued R., Smyth S.J., Phillips P.W.B. and Hesseln H. (2018): **Regulatory Uncertainty Around New Breeding Techniques.** Front. Plant Sci. | https://doi.org/10.3389/fpls.2018.01291
Emerging precision breeding techniques have great potential to develop new crop varieties with specific traits that can contribute to ensuring future food security in a time of increasing climate change pressures, such as disease, insects and drought. These techniques offer options for crop trait development in both private and public sector breeding programs. Yet, the success of new breeding techniques is not guaranteed at the scientific level alone: political influences and social acceptance significantly contribute to how crops will perform in the market. Using survey data, we report results from an international panel of experts regarding the institutional and social barriers that might impede the development of new plant technologies. Survey results clearly indicate that regulatory issues, social, and environmental concerns are critical to the success of precision breeding. The cross-regional analysis shows heterogeneity between Europeans and North Americans, particularly regarding political attitudes and social perceptions of targeted breeding techniques.
https://www.frontiersin.org/articles/10.3389/fpls.2018.01291/full

Lassoued R., Macall D.M., Hesseln H., Phillips P.W.B., Smyth S.J. (2019): **Benefits of genome-edited crops: expert opinion.** Transgenic Res. | https://doi.org/10.1007/s11248-019-00118-5
Innovation in agriculture is pervasive. However, in spite of the success stories of twentieth century plant breeding, the twenty-first century has ushered in a set of challenges that solutions from the past century are unlikely to address. However, sustained research and the amalgamation of a number of disciplines has resulted in new breeding techniques (NBTs), such as genome editing, which offer the promise of new opportunities to resolve some of the issues. Here we present the results of an expert survey on the added potential benefits of genome-edited crops compared to those developed through genetic modification (GM) and conventional breeding. Overall, survey results reveal a consensus among experts on the enhanced agronomic performance and product quality of genome-edited crops over alternatives. The majority of experts indicated that the regulations for health and safety, followed by export markets, consumers, and the media play a major role in determining where and how NBTs, including genome editing, will be developed and used in agriculture. Further research is needed to

gauge expert opinion after the Court of Justice of the European Union ruling establishing that site-specific mutagenic breeding technologies are to be regulated in the same fashion as GM crops, regardless of whether foreign DNA is present in the final variety.
https://link.springer.com/article/10.1007/s11248-019-00118-5

Lassoued R., Macall D.M., Smyth S.J., Phillips P.W.B., Hesseln H. (2020): **How should we regulate products of new breeding techniques? Opinion of surveyed experts in plant biotechnology.** Biotechnology Reports | https://doi.org/10.1016/j.btre.2020.e00460
The adoption of genome editing depends among others, on a clear and navigable regulatory framework that renders consistent decisions. Some countries like the United States decided to deregulate specific transgene-free genome edited products that could be created through traditional breeding and are not considered to be plant pests, while others are still challenged to fit emerging technologies in their regulatory system. Here we poll international experts in plant biotechnology on what approach should nations agree upon to accommodate current and future new breeding technologies and derived products. A key finding is product-based models or dual-product/process systems are viewed as potential appropriate frameworks to regulate outcomes of genome editing. As regulation of novel products of biotechnology is expected to impact research and trade, we test the impact of experts' worldviews on these issues. Results show that region influences worldviews of trade but not of agricultural innovation. In contrast, there was no effect of experts' worldviews on how products of novel biotechnologies should be regulated.
https://www.sciencedirect.com/science/article/pii/S2215017X19306599?via%3Dihub
https://reader.elsevier.com/reader/sd/pii/S2215017X19306599?token=A1C83D0FC3A85370528DD79CFB871EDE6602C85DBBEF42D74AB5E94E227E63F21D3A70B9EB137B5F580264A00E32F399

Lassoued R., Phillips P.W.B., Macall D.M., Hesseln H., Smyth S. J. (2021): **Expert opinions on the regulation of plant genome editing.** Plant Biotechnology J. **|** https://doi.org/10.1111/pbi.13597
Global food security is largely affected by factors such as: environmental (e.g. drought, flooding), social (e.g. gender inequality), socio-economic (e.g. overpopulation, poverty) and health (e.g. diseases). In response, extensive public and private investment in agricultural research has focused on increasing yields of staple food crops and developing new traits for crop improvement. New breeding techniques pioneered by genome editing have gained substantial traction within the last decade, revolutionizing the plant breeding field. Both industry and academia have been investing and working to optimize the potentials of gene editing and to bring derived crops to market. The spectrum of cutting-edge genome editing tools along with their technical differences has led to a growing international regulatory, ethical and societal divide. This article is a summary of a multi-year survey project exploring how experts view the risks of new breeding techniques, including genome editing and their related regulatory requirements. Surveyed experts opine that emerging biotechnologies offer great promise to address social and climate challenges, yet they admit that the market growth of genome-edited crops will be limited by an ambiguous regulatory environment shaped by societal uncertainty.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/pbi.13597
https://onlinelibrary.wiley.com/doi/10.1111/pbi.13597?af=R

Lema M.A. (2019): **Regulatory aspects of gene editing in Argentina.** Transgenic Res (2019) 28:147–150 | https://doi.org/10.1007/s11248-019-00145-2
Argentina is a world leader in regards to regulation and adoption of genetically modified (GM)crops. As a consequence, the regulatory aspects of gene editing applied to agriculture were considered proactively by the Argentinian regulators, who implemented simple but solid pioneering regulatory criteria for gene edited crops. At present, the Argentine regulatory system is fully able to establish if a gene-edited crop should be classified (and handled) either as a GM crop or a conventional new variety. To this end, the concept of ''novel combination of genetic material'' derived from the Cartagena Protocol on Biosafety is of decisive importance. After some pilot cases that have been managed under this criteria, now applicants appreciate the ease, speed and predictability of the regulation. Moreover, it has been considered by other countries in the course of developing their own regulations, thus acting also as a harmonization factor for the safe and effective insertion of these technologies in the global market.
https://link.springer.com/content/pdf/10.1007%2Fs11248-019-00145-2.pdf

Li J., Zhang S., Zhang R, Gao., Qi Y et al. (2020): **Efficient multiplex genome editing by CRISPR/Cas9 in common wheat.** Plant Biotechnology Journal | DOI: 10.1111/pbi.13508
Common wheat has a large genome with three subgenomes (A, B and D), making it challenging to create mutations at multiple genomic sites simultaneously. The CRISPR/Cas9 system offers a game changing tool for editing crop genomes (Chen et al., 2019). Three main strategies have been developed to produce multiple single guide RNAs (sgRNAs), including the conventional multiplex system with tandem repeats of separate U3 or U6 promoters (TRSP), the tRNA processing system (Xie et al., 2015), and the ribozyme processing system (Gao and Zhao, 2014).
https://europepmc.org/article/med/33150679

Mackelprang R. and Lemaux P.G. (2020): **Genetic Engineering and Editing of Plants: An Analysis of New and Persisting Questions, Annual Review of Plant Biology** 71, 659-687 | https://doi.org/10.1146/annurev-arplant-081519-035916 finally published
Genetic engineering is a molecular biology technique that enables a gene or genes to be inserted into a plant's genome. The first genetically engineered plants were grown commercially in 1996, and the most common genetically engineered traits are herbicide and insect resistance. Questions and concerns have been raised about the effects of these traits on the environment and human health, many of which are addressed in a pair of 2008 and 2009 *Annual Review of Plant Biology* articles. As new science is published and new techniques like genome editing emerge, reanalysis of some of these issues, and a look at emerging issues, is warranted. Herein, an analysis of relevant scientific literature is used to present a scientific perspective on selected topics related to genetic engineering and genome editing.
https://www.annualreviews.org/doi/pdf/10.1146/annurev-arplant-081519-035916

Marette S., Disdier A.-C., Beghin J.C (2020): **A Comparison of EU and US consumers' willingness to pay for gene-edited food: Evidence from apples.** Appetite | https://doi.org/10.1016/j.appet.2020.105064
We compare consumers' attitude towards and willingness to pay (WTP) for gene-edited (GE) apples in Europe and the US. Using hypothetical choices in a lab and different technology messages, we estimate WTP of 162 French and 166 US consumers for new apples, which do not brown upon being sliced or cut. Messages center on (i) the social and private benefits of having the new apples, and (ii) possible technologies leading to this new benefit (conventional hybrids, GE, and genetically modified (GMO)). French consumers do not value the innovation and actually discount it when it is generated via biotechnology. US consumers do value the innovation as long as it is not generated by biotechnology. In both countries, the steepest discount is for GMO apples, followed by GE apples. Furthermore, the discounting occurs through "boycott" consumers who dislike biotechnology. However, the discounting is weaker for US consumers compared to French consumers. Favorable attitudes towards sciences and new technology totally offset the discounting of GE apples.
https://www.sciencedirect.com/science/article/abs/pii/S019566632031686X?dgcid=rss_sd_all

Menz J., Modrzejewski D., Hartung F., Wilhelm R., Sprink T. (2020): **Genome Edited Crops Touch the Market: A View on the Global Development and Regulatory Environment.** Front. Plant Sci. 11:586027 | https://doi.org/10.3389/fpls.2020.586027
Products of genome editing as the most promising "New Plant Breeding Technology" (NPBT) have made the transition from the lab to the market in a short time. Globally, research activities employing genome editing are constantly expanding and more and more plants with market-oriented traits are being developed, and companies have already released the first genome edited crops to the market. Few countries, most of which are located in the Americas, have adapted legislations to these technologies or released guidelines supporting the use of genome editing. Other countries are debating the path to come either because there is no clarity on the legal classification or due consensus is hampered by a renewed GMO debate. In recent years (2017−2020), eight countries have introduced guidelines clarifying the legal status of genome edited products and many of those are actively committed to international harmonization of their policies. In this publication we give an overview on the current and potentially future international regulatory environment and an update on plants derived by genome editing with market-oriented traits.
https://www.frontiersin.org/articles/10.3389/fpls.2020.586027/full

Metje-Sprink J, Menz J, Modrzejewski D and Sprink T (2019): **DNA-Free Genome Editing: Past, Present and Future. Front.** Plant Sci. 9:1957 | doi: 10.3389/fpls.2018.01957
Genome Editing using engineered endonuclease (GEEN) systems rapidly took over the field of plant science and plant breeding. So far, Genome Editing techniques have been applied in more than fifty different plants; including model species like Arabidopsis; main crops like rice, maize or wheat as well as economically less important crops like strawberry, peanut and cucumber. These techniques have been used for basic research as proof-of-concept or to investigate gene functions in most of its applications. However, several market-oriented traits have been addressed including enhanced agronomic characteristics, improved food and feed quality, increased tolerance to abiotic and biotic stress and herbicide tolerance. These technologies are evolving at a tearing pace and especially the field of CRISPR based Genome Editing is advancing incredibly fast. CRISPR-Systems derived from a multitude of bacterial species are being used for targeted Gene Editing and many modifications have already been applied to the existing CRISPR-Systems such as (i) alter their protospacer adjacent motif (ii) increase their specificity (iii) alter their ability to cut DNA and (iv) fuse them with additional proteins. Besides, the classical transformation system using *Agrobacteria tumefaciens* or *Rhizobium rhizogenes*, other transformation technologies have become available and additional methods are on its way to the plant sector. Some of them are utilizing solely proteins or protein-RNA complexes for transformation, making it possible to alter the genome without the use of recombinant DNA. Due to this, it is impossible that foreign DNA is being incorporated into the host genome. In this review we will present the recent developments and techniques in the field of DNA-free Genome Editing, its advantages and pitfalls and give a perspective on technologies which might be available in the future for targeted Genome Editing in plants. Furthermore, we will discuss these techniques in the light of existing– and potential future regulations. https://www.frontiersin.org/articles/10.3389/fpls.2018.01957/full

Metje-Sprink J., Sprink T., Hartung F. (2020): **Genome-edited plants in the field.** Current Opinion in Biotechnology, 61, 1–6 | https://doi.org/10.1016/j.copbio.2019.08.007

The application of site directed nucleases (SDN) for Genome Editing (GE) in plant breeding and research increases exponentially in the last few years. The main research so far was on 'proof of concept' studies or improvement of the precision and delivery of the SDN. Nevertheless, a reasonable amount of research is present on market-oriented applications for cash crops such as rice but also for commercially lesser interesting crops and vegetables. Reported field trials involving GE plants are scarce around the world and almost not existing in Europe. This is due to the regulatory landscape for GE plants, which is quite distinct and especially in the European Union very demanding. By far the most field trials involve GE rice varieties in the Asian area, followed up by tomato and other vegetables and crops.
https://reader.elsevier.com/reader/sd/pii/S0958166919300618?token=452393C7172172D07A3B3CC1645F7FA72D4357C63221749134269F691910E0F5DE4053C16D94D3B0E5A98AC4805FE5FD

Meyer, M., Heimstädt, C. (2019): **The divergent governance of gene editing in agriculture: a comparison of institutional reports from seven EU member states.** Plant Biotechnol Rep 13, 473–482 | https://doi.org/10.1007/s11816-019-00578-5

How have national institutions and committees from EU member states positioned themselves regarding the use of gene editing in agriculture? To answer this question, this article examines and compares 11 official reports and position statements from 7 European countries: Germany, France, the Netherlands, Italy, Spain, Denmark, and Sweden. The various kinds of issues that are addressed and arguments that are made in the reports are coded into large categories (innovation, risk, ethics, legislation, etc.) and are analyzed. The paper discusses the main similarities and differences in terms of how the governance of gene editing is problematized. In doing so, the paper aims to provide a useful resource to broaden debates on the future regulation of gene editing within and beyond Europe.
https://link.springer.com/article/10.1007/s11816-019-00578-5

Modrzejewski, D., Hartung, F., Sprink, T. et al.(2019): **What is the available evidence for the range of applications of genome-editing as a new tool for plant trait modification and the potential occurrence of associated off-target effects: a systematic map**. *Environ Evid* **8,** 27 | https://doi.org/10.1186/s13750-019-0171-5

Background: Within the last decades, genome-editing techniques such as CRISPR/Cas, TALENs, Zinc-Finger Nucleases, Meganucleases, Oligonucleotide-Directed Mutagenesis and base editing have been developed enabling a precise modification of DNA sequences. Such techniques provide options for simple, time-saving and cost-effective applications compared to other breeding techniques and hence genome editing has already been promoted for a wide range of plant species. Although the application of genome-editing induces less unintended modifications (off-targets) in the genome compared to classical mutagenesis techniques, off-target effects are a prominent point of criticism as they are supposed to cause unintended effects, e.g. genomic instability or cell death. To address these aspects, this map aims to answer the following question: What is the available evidence for the range of applications of genome-editing as a new tool for plant trait modification and the potential occurrence of associated off-target effects? This primary question will be considered by two secondary questions: One aims to overview the market-oriented traits being modified by genome-editing in plants and the other explores the occurrence of off-target effects.
Methods: A literature search in nine bibliographic databases, Google Scholar, and 47 web pages of companies and governmental agencies was conducted using predefined and tested search strings in English language. Articles were screened on title/abstract and full text level for relevance based on pre-defined inclusion criteria. The relevant information of included studies were mapped using a pre-defined data extraction strategy. Besides a descriptive summary of the relevant literature, a spreadsheet containing all extracted data is provided.
Results: Altogether, 555 relevant articles from journals, company web pages and web pages of governmental agencies were identified containing 1328 studies/applications of genome-editing in model plants and agricultural crops in the period January 1996 to May 2018. Most of the studies were conducted in China followed by the USA. Genome-editing was already applied in 68 different plants. Although most of the studies were basic research, 99 different market-oriented applications were identified in 28 different crops leading to plants with improved food and feed quality, agronomic value like growth characteristics or increased yield, tolerance to biotic and abiotic stress, herbicide tolerance or industrial benefits. 252 studies explored off-target effects. Most of the studies were conducted using CRISPR/Cas. Several studies firstly investigated whether sites in the genome show similarity to the target sequence and secondly analyzed these potential off-target sites by sequencing. In around 3% of the analyzed potential off-target
https://environmentalevidencejournal.biomedcentral.com/track/pdf/10.1186/s13750-019-0171-5

Modrzejewski D., Hartung F., Lehnert H., Sprink T., Kohl C., Keilwagen J. and Wilhelm R. (2020): **Which Factors Affect the Occurrence of Off-Target Effects Caused by the Use of CRISPR/Cas: A Systematic Review in Plants.** Front. Plant Sci. 11:574959. | doi: 10.3389/fpls.2020.574959

CRISPR/Cas enables a targeted modification of DNA sequences. Despite their ease and efficient use, one limitation is the potential occurrence of associated off-target effects. This systematic review aims to answer the following research question: Which factors affect the occurrence of off-target effects caused by the use of CRISPR/Cas in plants? Literature published until March 2019 was considered for this review. Articles were screened for relevance based on pre-defined inclusion criteria. Relevant studies were subject to critical appraisal. All studies included in the systematic review were synthesized in a narrative report, but studies rated as

high and medium/high validity were reported separately from studies rated as low and medium/low or unclear validity. In addition, we ran a binary logistic regression analysis to verify five factors that may affect the occurrence of off-target effects: (1) Number of mismatches (2) Position of mismatches (3) GC-content of the targeting sequence (4) Altered nuclease variants (5) Delivery methods. In total, 180 relevant articles were included in this review containing 468 studies therein. Seventy nine percentage of these studies were rated as having high or medium/high validity. Within these studies, 6,416 potential off-target sequences were assessed for the occurrence of off-target effects. Results clearly indicate that an increased number of mismatches between the on-target and potential off-target sequence steeply decreases the likelihood of off-target effects. The observed rate of off-target effects decreased from 59% when there is one mismatch between the on-target and off-target sequences toward 0% when four or more mismatches exist. In addition, mismatch/es located within the first eight nucleotides proximal to the PAM significantly decreased the occurrence of off-target effects. There is no evidence that the GC-content significantly affects off-target effects. The database regarding the impact of the nuclease variant and the delivery method is very poor as the majority of studies applied the standard nuclease SpCas9 and the CRISPR/Cas system was stably delivered in the genome. Hence, a general significant impact of these two factors on the occurrence of off-target effects cannot be proved. This identified evidence gap needs to be filled by systematic studies exploring these individual factors in sufficient numbers.
https://www.readcube.com/articles/10.3389/fpls.2020.574959

Moldenhauer H., Brockmann K. Bannier H.-J, Häusling M. (2019): **ZUKUNFT ODER ZEITBOMBE? - DESIGNERPFLANZEN ALS ALLHEILMITTEL SIND NICHT DIE LÖSUNG!**:
https://www.martin-haeusling.eu/images/DESIGNERPFLANZEN_mit_CRISPR_und_Co_Haeusling_Web_RZ.pdf
Im Auftrag der Grünen/EFA, im Wesentlichen politisch ausgerichtet

Myskja B.K. and Myh A.I. (2020): **Non-safety Assessments of Genome-Edited Organisms: Should They be Included in Regulation?** Science and Engineering Ethics | https://doi.org/10.1007/s11948-020-00222-4
This article presents and evaluates arguments supporting that an approval procedure for genome-edited organisms for food or feed should include a broad assessment of societal, ethical and environmental concerns; so-called non-safety assessment. The core of analysis is the requirement of the Norwegian Gene Technology Act that the sustainability, ethical and societal impacts of a genetically modified organism should be assessed prior to regulatory approval of the novel products. The article gives an overview how this requirement has been implemented in the regulatory practice, demonstrating that such assessment is feasible and justified. Even in situations where genome-edited organisms are considered comparable to non-modified organisms in terms of risk, the technology may have—in addition to social benefits—negative impacts that warrant assessments of the kind required in the Act. The main reason is the disruptive character of the genome editing technologies due to their potential for novel, ground-breaking solutions in agriculture and aquaculture combined with the economic framework shaped by the patent system. Food is fundamental for a good life, biologically and culturally, which warrants stricter assessment procedures than what is required for other industries, at least in countries like Norway with a strong tradition for national control over agricultural markets and breeding programs.
https://link.springer.com/content/pdf/10.1007/s11948-020-00222-4.pdf

Nature Biotechnology Editorial (2018): **Gene-edited plants cross European event horizon.** Nature Biotechnology 36, (9), 776
By lumping gene-edited plants together with other genetically modified organisms (GMOs), Europe's highest court has consigned this plant-breeding approach to a regulatory black hole.
https://www.nature.com/articles/nbt.4256

Nature Editorial: **Revamp of UK CRISPR regulation will require public trust**. Nature **591**, 345 (2021) | doi: https://doi.org/10.1038/d41586-021-00672-1
The United Kingdom is considering innovative ways of regulating gene editing in food and farming. Robust processes and public confidence will be vital for success.
https://www.nature.com/articles/d41586-021-00672-1

Nakayasu M. et al. (2018): **Generation of a-solanine-free hairy roots of potato by CRISPR/Cas9 mediated genome editing of the St16 DOX gene.** Plant Physiol. Biochem. 131, 70–77
Potato (*Solanum tuberosum*) is a major food crop, while the most tissues of potato accumulates steroidal glycoalkaloids (SGAs) α-solanine and α-chaconine. Since SGAs confer a bitter taste on human and show the toxicity against various organisms, reducing the SGA content in the tubers is requisite for potato breeding. However, generation of SGA-free potato has not been achieved yet, although silencing of several SGA biosynthetic genes led a decrease in SGAs. Here, we show that the knockout of *St16DOX* encoding a steroid 16α-hydroxylase in SGA biosynthesis causes the complete abolition of the SGA accumulation in potato hairy roots. Nine candidate guide RNA (gRNA) target sequences were selected from *St16DOX* by *in silico* analysis, and the two or three gRNAs were introduced into a CRISPR/Cas9 vector designated as pMgP237-2A-GFP that can express multiplex gRNAs based on the pre-tRNA processing system. To establish rapid screening of the candidate gRNAs that can efficiently mutate the *St16DOX* gene, we used a potato hairy root culture system for the introduction of the pMgP237 vectors. Among the transgenic hairy roots, two independent lines showed no detectable SGAs but accumulated the glycosides of 22,26-dihydroxycholesterol, which is the substrate of St16DOX. Analysis of the

two lines with sequencing exhibited the mutated sequences of *St16DOX* with no wild-type sequences. Thus, generation of SGA-free hairy roots of tetraploid potato was achieved by the combination of the hairy root culture and the pMgP237-2A-GFP vector. This experimental system is useful to evaluate the efficacy of candidate gRNA target sequences in the short-term.
https://www.sciencedirect.com/science/article/abs/pii/S0981942818301840?via%3Dihub

Nazir S., Iqbal Z.I. and Sajid-ur-Rahman (2019**): Molecular Identification of Genetically Modified Crops for Biosafety and Legitimacy of Transgenes.**
| *DOI: http://dx.doi.org/10.5772/intechopen.81079*
Crops undergo artificially DNA modifications for improvements are considered as genetically modified (GM) crops. These modifications could be in indigenous DNA or by introduction of foreign DNA as transgenes. There are 29 different crops and fruit trees in 42 countries, which have been successfully modified for various traits like herbicide tolerance, insect/pest resistance, disease resistance and quality improvement. GM crops are grown worldwide and its area is significantly increasing every year. Many countries have very strict rules and regulations for GM crops and are also a trade barrier in some situations. Hence, identification and testing of crops for GM contents is important for identity and legitimacy of transgene to simplify the international trade. Normally, molecular identification is performed at three different levels, i.e., DNA, RNA and protein, and each level has its own importance in testing about the nature and type of GM crops. In this chapter, current scenario of GM crops and different molecular testing tools are described in brief.

Nogue´ F., Vergne P., Che`vre A._M., Chauvin J.-E. et al. (2019): Crop plants with improved culture and quality traits for food, feed and other uses. Transgenic Res (2019) 28:65–73 | https://doi.org/10.1007/s11248-019-00135-4
The large French research project GENIUS (2012–2019, https://www6.inra.genius-project_eng/) provides a good showcase of current genome editing techniques applied to crop plants. It addresses a large variety of agricultural species (rice, wheat, maize, tomato, potato, oilseed rape, poplar, apple and rose) together with some models (Arabidopsis, Brachypodium, Physcomitrella). Using targeted mutagenesis as its work horse, the project is limited to proof of concept under confined conditions. It mainly covers traits linked to crop culture, such as disease resistance to viruses and fungi, flowering time, plant architecture, tolerance to salinity and plant reproduction but also addresses traits improving the quality of agricultural products for industrial purposes. Examples include virus resistant tomato, early flowering apple and low-amylose starch potato. The wide range of traits illustrates the potential of genome editing towards a more sustainable agriculture through the reduction of pesticides and to the emergence of innovative bio-economy sectors based on custom tailored quality traits.
https://link.springer.com/article/10.1007/s11248-019-00135-4

Noleppa S., Cartsburg M. (2021): **The socio-economic and environmental values of plant breeding in the EU and for selected EU member states**.
HFFA Research Paper 2021 | https://hffa-research.com/wp-content/uploads/2021/05/HFFA-Research-The-socio-economic-and-environmental-values-of-plant-breeding-in-the-EU.pdf

Parrott W.A., Harbell J., Kaeppler H., Jones T., Tomes D., Van Eck J., Wang K., Wenck A. (2020): **The proposed APHIS regulation modernization could enhance agriculture biotechnology research and development in the USA**
In Vitro Cell.Dev.Biol.-Plant | https://doi.org/10.1007/s11627-019-10039-x
The USDA's Animal and Plant Health Inspection Service (APHIS) is one of three agencies that govern the importation, interstate movement, or environmental release of certain genetically engineered (GE) organisms. APHIS regulations are in 7 CFR part 340, originally issued in 1987 (https://www.aphis.usda.gov/biotechnology/downloads/7_cfr_340.pdf) and based on the premise that a GE crop could pose a plant pest risk. A major revision was proposed June 6, 2019 (https://www.aphis.usda.gov/brs/fedregister/BRS_20190606.pdf), with public comments accepted for 60 d. Members of the Society for *In Vitro* Biology (SIVB)—especially within the plant section—are impacted by the current rules and will be impacted by changes. Therefore, the public policy committee studied the changes and prepared a response that was reviewed by the board of directors and submitted to APHIS. APHIS received 6186 comments overall. In general, the SIVB welcomes the proposed revisions, which recognize established scientific guidelines and principles for plant pest risk assessment. In addition, they recognize the safety record accumulated over multiple decades of current GE mechanisms of action (MOA), so the proposed rules include an exemption for new events with established MOA's in a previously reviewed crop. Further, the proposed rules focus on DNA function and impact rather than its source organism with regulatory review triggered by potential for increased plant pest risk. Most importantly, the proposed revisions codify a light regulatory approach for many applications of genome editing, because these applications result in plants that could otherwise have been developed through traditional breeding techniques or found in nature. If implemented appropriately in the final rule, we find these changes remove many current barriers, and thus are likely to stimulate university and business "startup" innovation. The SIVB recognizes the need for exemption for further model species and gene delivery organisms. Such concerns were adequately expressed by the submitted response. Remaining hurdles for innovative plant incorporated protectants are still problematic. Nevertheless, the SIVB applauds the efforts to update APHIS rules in a scientifically defensible manner. The detailed response is shared below.
https://link.springer.com/content/pdf/10.1007%2Fs11627-019-10039-x.pdf

Parisi, C. and Rodriguez Cerezo, E., **Current and future market applications of new genomic techniques**, EUR 30589 EN, Publications Office of the European Union, Luxembourg, 2021, ISBN 978-92-76-30206-3, doi:10.2760/02472 , JRC123830.
This report presents a review of market applications of new genomic techniques (NGTs). For the purposes of this study, NGTs are defined as 'techniques that are able to alter the genetic material of an organism, developed after the publication of EU Directive 2001/18/EC'.
The study covers NGT applications in agri-food, industrial and medicinal sectors that have resulted in applications that are already being marketed, are at a confirmed pre-market development stage or are at a research and development (R & D) stage but showing market potential. The scope includes the use of NGTs in any kind of plant, mushroom, animal or microorganism or in human cells.
Data on NGT applications were collected from multiple sources, including information available online, consultation of experts and an ad hoc survey of public and private technology developers. The NGT applications identified were classified, using the information available, as being at the following development stages.
• **Commercial stage.** NGT applications currently marketed in at least one country worldwide.
• **Pre-commercial stage.** NGT applications ready to be commercialised in at least one country worldwide but not yet on the market (commercialisation mainly depends on the developer's decision and a 5-year horizon is estimated).
• **Advanced R & D stage.** NGT applications at a late stage of development (field trials in the case of plants, *in*/*ex vivo* clinical trials in the case of medical applications) and likely to reach the market in the medium term (i.e. by 2030).
• **Early R & D stage.** NGT applications at proof of concept stage (i.e. testing gene targets for trait enhancement of commercial interest).
NGTs, especially those based on clustered regularly interspaced short palindromic repeats (CRISPR), are being actively and increasingly used in all the sectors analysed. Currently, few NGT applications are marketed worldwide: one plant product, one microorganism for release into the environment and several microorganisms used for contained production of commercial molecules. There are, however, about 30 identified applications (in plants, animals and microorganisms) at a pre-commercial stage in the pipeline that could reach the market in the short term (within 5 years). In addition, the medicinal sector is actively using NGTs to tackle several human diseases, and in many cases applications have already reached patients, in phase I and phase I/II clinical trials.

POORTVLIET P.M., PURNHAGEN K.P., BOERSMA R. and GREMMEN B. (2019): **On the Legal Categorisation of New Plant Breeding Technologies: Insights from Communication Science and Ways Forward.** European Journal of Risk Regulation | https://doi.org/10.1017/err.2019.10
In July 2018 the Court of Justice of the European Union (CJEU) ruled that organisms obtained from most New Plant Breeding Technologies (NPBT) fulfil the requirements of the GMO definition of Directive 2001/18. Practically, organisms created with NPBT have since been legally treated as GMOs. While we do not seek to contest the judgment in itself, in the present contribution we draw attention to the effects of such a categorisation from the perspective of communication science. Extrapolating from communication research conducted in adjacent technology domains, we will argue that by putting organisms obtained from NPBT semantically in the same basket as GMOs may carry a serious risk – transferring analogous communication problems that GMOs encountered in the past, to organisms obtained from NPBT, while they may not address similar risks. Possible consequences such as these can hardly be considered at the stage of legal interpretation (such as with the CJEU). Rather, as discussion now unfolds whether and how to change the legal definition, insights from communication science and risk perception research on the effect of such a definition should be taken into account.
https://www.cambridge.org/core/journals/european-journal-of-risk-regulation/article/on-the-legal-categorisation-of-new-plant-breeding-technologies-insights-from-communication-science-and-ways-forward/A8404A3F4C4FE28A9C1F50A05EE2BA6E
and
http://www.ask-force.org/web/Genomics/Poortviliet-On-the-legal-categorisation-of-New-Plant-Breeding-Technologies-Insights-from-communication-science-and-ways-forward-2018.pdf

Posthof C. (2018): **EuGH stärkt Vorsorge.** Genethischer Informationsdienst 246, 26-27
Der Europäische Gerichtshof (EuGH) hat sich in seinem Urteil vom 25.Juli zu der Regulierung neuer Gentechnik-Verfahren geäußert. Die RichterInnen vertreten die Ansicht, dass das derzeit gültige EU-Recht auch auf neue Gentechnik-Verfahren anwendbar ist – eine gute Nachricht für die Gentechnik-kritische Bewegung.

Purnhagen K.P, Kok E., Kleter G., Schebesta H., Visser R.G.F. and Wesseler J. (2018) **EU court casts new plant breeding techniques into regulatory limbo.** Nature Biotechnology 36, 799–800
We note that the CJEU is legally not allowed to go on a fact-finding mission. The judges interpret the materials presented to them by the referring court and the (public) parties consulted.
https://www.nature.com/articles/nbt.4251

Purnhagen K.P. and Wesseler J.H.H. (2019): **Maximum vs minimum harmonization: what to expect from the institutional and legal battles in the EU on gene editing technologies.** Pest Management Science | https://doi.org/10.1002/ps.5367

New plant-breeding technologies (NPBTs), including gene editing, are widely used and drive the development of new crops. However, these new technologies are disputed, creating uncertainty in how their application for agricultural and food uses will be regulated. While in North America regulatory systems respond with a differentiated approach to NPBTs, the Court of Justice of the European Union (EU) has in effect made most if not all NPBT subject to the same regulatory regime as genetically modified organisms (GMOs). This paper discusses from a law and economics point of view different options that are available for the EU's multi-level legal order. Using an ex-ante regulation versus ex-post liability framework allows the economic implications of different options to be addressed. The results show that under current conditions, some options are more expensive than others. The least costly option encompasses regulating new crops derived from NPBTs similar to those used in 'conventional' breeding. The current regulatory situation in the EU, namely making the use of NPBTs subject to the same conditions as GMOs, is the most costly option.
https://onlinelibrary.wiley.com/doi/full/10.1002/ps.5367

Purnhagen K. (2019): **How To Manage The Union´s Diversity: The Regulation Of New Plant Breeding Technologies In Confédération Paysanne And Other.** 56 *Common Market Law Review*, Issue 5, 1379–1396
http://www.kluwerlawonline.com/abstract.php?area=Journals&id=COLA2019106

Purnhagen K., Wesseler J. (2020): **EU Regulation of New Plant Breeding Technologies and Their Possible Economic Implications for the EU and Beyond.** Applied Economic Perspectives and Policy |
https://doi.org/10.1002/aepp.13084
New plant breeding technologies (NPBTs), including CRISPR gene editing, are being used widely, and they are driving the development of new crops. They are nevertheless a subject of criticism and discussion. According to a summer 2018 interpretation by the Court of Justice of the European Union (CJEU) applying an absolute interpretation of the precautionary principle, European Union (EU) law makes most NPBTs subject to regulations governing the use of genetically modified organisms (GMOs) in the EU. This contribution summarizes the status of the debate and highlights issues that have thus far not been considered—particularly with regard to the implications of EU regulations for NPBTs for countries outside the EU.
https://onlinelibrary.wiley.com/doi/epdf/10.1002/aepp.13084

Qaim, M. (2020). **Role of new plant breeding technologies for food security and sustainable agricultural development.** Applied Economic Perspectives and Policy
| https://doi.org/10.1002/aepp.13044
New plant breeding technologies (NPBTs), including genetically modified and gene-edited crops, offer large potentials for sustainable agricultural development and food security while addressing shortcomings of the Green Revolution. This article reviews potentials, risks, and actually observed impacts of NPBTs. Regulatory aspects are also discussed. While the science is exciting and some clear benefits are already observable, overregulation and public misperceptions may obstruct efficient development and use of NPBTs. Overregulation is particularly observed in Europe, but also affects developing countries in Africa and Asia, which could benefit the most from NPBTs. Regulatory reforms and a more science-based public debate are required.
https://onlinelibrary.wiley.com/doi/epdf/10.1002/aepp.13044

Ribarits, A., Narendja, F., Stepanek, W., Hochegger, R. (2021): **Detection Methods Fit-for-Purpose in Enforcement Control of Genetically Modified Plants Produced with Novel Genomic Techniques (NGTs)**. Agronomy 11, 61. | https://doi.org/10.3390/agronomy11010061
The comprehensive EU regulatory framework regarding GMOs aims at preventing damage to human and animal health and the environment, and foresees labelling and traceability. Genome-edited plants and products fall under these EU GMO regulations, which have to be implemented in enforcement control activities. GMO detection methods currently used by enforcement laboratories are based on real-time PCR, where specificity and sensitivity are important performance parameters. Genome editing allows the targeted modification of nucleotide sequences in organisms, includingplants, and often produces single nucleotide variants (SNVs), which are the most challenging class of genome edits to detect. The test method must therefore meet advanced requirements regarding specificity, which can be increased by modifying a PCR method. Digital PCR systems achieve a very high sensitivity and have advantages in quantitative measurement. Sequencing methods may also be used to detect DNA modifications caused by genome editing. Whereas most PCR methods can be carried out in an enforcement laboratory with existing technical equipment and staff, the processing of the sequencing data requires additional resources and the appropriate bioinformatic expertise
https://www.mdpi.com/2073-4395/11/1/61

May have also look on: Gocht A., Consmüller N., Thom F., Grethe H. (2020): Economic and Environmental Consequences of the ECJ Genome Editing Judgement in Agriculture. Thünen Working Paper 150
https://literatur.thuenen.de/digbib_extern/dn062466.pdf

Ricroch A. (2019): **Global developments of genome editing in agriculture.** Transgenic Res 28 (Suppl 2): 45-52 | https://doi.org/10.1007/s11248-019-00133-6
Genome editing, particularly using of site-directed nucleases such as the CRISPR system, has spread rapidly through the biological sciences. Genome editing in crops could significantly speed up the progress of breeding

programs. It could drive the development of traits in new crops and allow improvements in yield and pest resistance, adaptation to climate change, and industrial and pharmaceutical applications. However, biofortification is a key challenge to satisfy nutritional needs in vitamins for developing countries and new consumer's needs for developed countries. China and the USA lead scientific research in crop editing. Nigeria, being headquarters to numerous research consortia, is the most involved country in Africa. Genome editing in animals including pig, cattle, sheep, and carp, has not merely accelerated research but has made possible research that was previously unfeasible. It has been used to increase disease resistance, to make livestock better adapted to farming or environmental conditions, to increase fertility and growth, and to improve animal welfare. The USA, the UK and China are the most involved countries in animal genome editing. Global food production needs to increase as much as 70 per cent to support the growing population. Genome editing could contribute improving the efficiency of food distribution and reducing waste. Depending on the regulatory conditions, genome editing could open up the field to smaller companies and public labs.
https://link.springer.com/content/pdf/10.1007%2Fs11248-019-00133-6.pdf

Ricroch A. (2020): **The place of Europe in the new plant breeding landscape: evolution of field trials**
CRISPR-cas gene editing in crop plants could significantly speed up the progress of breeding programs. Strikingly in the agricultural sector, the number of CRISPR-cas patents originating from Europe trails far behind the USA and China. Examining field trials is another mean to compile biotechnological innovation in plant breeding. We examined field trials since 2002 and more recently from 2015 to 2020 with the emergence of CRISPR-cas in plant breeding. A total of 881 field trials were conducted in the EU from 2002 to June 2020 and maize represents 54.3% of them. Disparities exist within the EU Member states and Spain leads the EU field trials with almost half of them. The drop of field trials in the EU since 2006 can be linked to strict GMO regulations. From January 2015 to June 2020, only 48 field trials were conducted, or are in progress, in eight countries compared to the 19 countries between 2002 and 2015. Spain and Sweden are ranking first with 28.3% of these field trials, while the UK is holding the third place with 17%. Only 5 field trials use CRISPR-Cas9. Agronomic improvement comes first, followed by nutritional enhancement and biotic stress resistance as traits of field trials. Regarding the biotech crops, potato is the most tested crop with a fifth of the field trials (20.8%). The implications of regulatory policy in the restrictive deployment of NBTs for plant improvement in Europe are discussed as well as the need for a new regulation.
https://www.europeanscientist.com/en/features/the-place-of-europe-in-the-new-plant-breeding-landscape-evolution-of-field-trials/

Rippe K.P. and Willemsen A (2018) The Idea of Precaution: **Ethical Requirements for the Regulation of New Biotechnologies in the Environmental Field**. Front. Plant Sci. 9:1868. | doi: 10.3389/fpls.2018.01868
The rapid emergence of new biotechnologies for selectively altering genetic material—so-called genome editing—has sparked public controversy about how their development and application in the environmental fields are to be regulated. Since the use of these new technologies harbors not only considerable potential but also risks of serious damage whose occurrence is uncertain due to their application in complex environmental systems, many national and international legal authorities are currently adhering to policies of precaution. According to critics, however, precautionary measures and the legal principle of precaution on which they are based are unduly restrictive in the case of the new biotechnologies, hindering advancements in both research and various fields of application. At the same time, legal notions of precaution are highly ambiguous within and across different national and international formulations, thereby further complicating the controversy about their implications. This paper goes beyond the concept of precaution as found in environmental law by examining the ethical significance and the ethical justification of precautionary measures in the environmental field. In particular, it clarifies the criterion of potential damage, disambiguates different types of epistemic bases in precaution decisions, and considers the relevance and implications of different ethical risk theories as to their response to epistemic uncertainty and vagueness. The two main conclusions are that, first, irrespective of the ethical risk theory embraced, there is an ethical obligation to take precautionary measures whenever serious damage is possible and the probability of damage occurring epistemically uncertain or vague. Regarding the risk assessment, it is argued that the burden of proof lies not with those who fear the occurrence of serious environmental damage. Rather, it is up to those whose actions give rise to such fears to demonstrate that serious damage is extremely improbable or scientifically absurd. Second, the moral responsibility to determine precaution situations and to specify appropriate precautionary measures is attributed not only to state authorities but also to industrial players as well as research communities. Based on these two conclusions, recommendations are given as to how the precautionary principle should be incorporated in political and legal decision-making.
http://www.readcube.com/articles/10.3389/fpls.2018.01868

Rönspies M., Schindele P. and Puchta H. (2020): **CRISPR/Cas-mediated chromosome engineering: opening up a new avenue for plant breeding.** *Journal of Experimental Botany*, eraa463, https://doi.org/10.1093/jxb/eraa463
The advent of powerful site-specific nucleases, particularly the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein (Cas) system, which enables precise genome manipulation, has revolutionized plant breeding. Until recently, the main focus of researchers has been to simply knock-in or knock-out single genes, or to induce single base changes, but constant improvements of this technology have enabled more ambitious applications that aim to improve plant productivity or other desirable traits. One longstanding aim has been the induction of targeted chromosomal rearrangements (crossovers, inversions, or

translocations). The feasibility of this technique has the potential to transform plant breeding, because natural rearrangements, like inversions, for example, typically present obstacles to the breeding process. In this way, genetic linkages between traits could be altered to combine or separate favorable and deleterious genes, respectively. In this review, we discuss recent breakthroughs in the field of chromosome engineering in plants and their potential applications in the field of plant breeding. In the future, these approaches might be applicable in shaping plant chromosomes in a directed manner, based on plant breeding needs.
https://academic.oup.com/jxb/advance-article-abstract/doi/10.1093/jxb/eraa463/6013291?redirectedFrom=fulltext

Rostoks N. (2021): **Implications of the EFSA Scientific Opinion on Site Directed Nucleases 1 and 2 for Risk Assessment of Genome-Edited Plants in the EU**. *Agronomy 11*(3), 572 | https://doi.org/10.3390/agronomy11030572
Genome editing is a set of techniques for introducing targeted changes in genomes. It may be achieved by enzymes collectively called site-directed nucleases (SDN). Site-specificity of SDNs is provided either by the DNA binding domain of the protein molecule itself or by RNA molecule(s) that direct SDN to a specific site in the genome. In contrast to transgenesis resulting in the insertion of exogenous DNA, genome editing only affects specific endogenous sequences. Therefore, multiple jurisdictions around the world have exempted certain types of genome-edited organisms from national biosafety regulations completely, or on a case-by-case basis. In the EU, however, the ruling of the Court of Justice on the scope of mutagenesis exemption case C-528/16 indicated that the genome-edited organisms are subject to the GMO Directive, but the practical implications for stakeholders wishing to develop and authorize genome-edited products in the EU remain unclear. European Food Safety Authority in response to a request by European Commission has produced a scientific opinion on plants developed by SDN-1, SDN-2, and oligonucleotide-directed mutagenesis (ODM) genome editing techniques. In this review, I will (1) provide a conceptual background on GMO risk assessment in the EU; (2) will introduce the main conclusions of the EFSA opinion, and (3) will outline the potential impact on the risk assessment of genome-edited plants.
https://www.mdpi.com/2073-4395/11/3/572/htm

Ruffell D. (2018): **The EU Court of Justice extends the GMO Directive to gene-edited organisms.** FEBS Letters 592, 3653–3657
https://febs.onlinelibrary.wiley.com/doi/epdf/10.1002/1873-3468.13293

Sánchez M.A.(2020): **Chile as a key enabler country for global plant breeding, agricultural innovation, and biotechnology**, GM Crops & Food,
| https://doi.org/10.1080/21645698.2020.1761757
Chile has become one of the main global players in seed production for counter-season markets and research purposes. Chile has a key role contributing to the reduction in seed productions hortages in the Northern Hemisphere by speeding up the development of new hybrids, cultivars, and genetically modified (GM) organisms. The seeds that Chile produces for export include a considerable amount of GM seeds. Between 2009 and 2018, 1,081 different seed-planting events were undertaken for seed multiplication and/or research purposes. Every single event that had commodity cultivation status in 2018 in at least one country underwent field activities in Chile at least once over the last 10 y. Chile just adopted a regulatory approach for new plant breeding techniques. This type of regulatory approach should contribute to maintaining the status of Chile as a hot spot for future innovation in plant breeding-based biotechnology
https://www.tandfonline.com/doi/pdf/10.1080/21645698.2020.1761757?needAccess=true

Schaart J.G., van de Weil C.C.M., Marinus J. M. Smulders M.J.M. (2021): **Genome editing of polyploid crops: prospects, achievements and bottlenecks.** Transgenic Res: | https://doi.org/10.1007/s11248-021-00251-0
Plant breeding aims to develop improved crop varieties. Many crops have a polyploid and often highly heterozygous genome, which may make breeding of polyploid crops a real challenge. The efficiency of traditional breeding based on crossing and selection has been improved by using marker-assisted selection (MAS), and MAS is also being applied in polyploid crops, which helps e.g. for introgression breeding. However, methods such as random mutation breeding are difficult to apply in polyploid crops because there are multiple homoeologous copies (alleles) of each gene. Genome editing technology has revolutionized mutagenesis as it enables precisely selecting targets. The genome editing tool CRISPR/Cas is especially valuable for targeted mutagenesis in polyploids, as all alleles and/or copies of a gene can be targeted at once. Even multiple genes, each with multiple alleles, may be targeted simultaneously. In addition to targeted mutagenesis, targeted replacement of undesirable alleles by desired ones may become a promising application of genome editing for the improvement of polyploid crops, in the near future. Several examples of the application of genome editing for targeted mutagenesis are described here for a range of polyploid crops, and achievements and bottlenecks are highlighted.
https://link.springer.com/content/pdf/10.1007/s11248-021-00251-0.pdf

Schiemann J., Dietz-Pfeilstetter A., Hartung F., Kohl C., Romeis J., and Thorben Sprink T. (2019): **Risk Assessment and Regulation of Plants Modified by Modern Biotechniques: Current Status and Future Challenges**. Annu. Rev. Plant Biol. 70, 699-726 | https://doi.org/10.1146/annurev-arplant-050718-100025
The review describes the current status and future challenges of risk assessment and regulation of plants modified by modern biotechniques, namely genetic engineering and genome editing. It provides a general overview of the biosafety and regulation of genetically modified plants and details different regulatory frameworks with a focus on the European situation. The environmental risk and safety assessment of genetically modified plants is explained, and aspects of toxicological assessments are discussed, especially the controversial debate in Europe on the added scientific value of untargeted animal feeding studies. Because RNA interference (RNAi) is increasingly explored for commercial applications, the risk and safety assessment of RNAi-based genetically modified plants is also elucidated. The production, detection, and identification of genome-edited plants are described. Recent applications of modern biotechniques, namely synthetic biology and gene drives, are discussed, and a short outlook on the future follows.
https://www.annualreviews.org/doi/10.1146/annurev-arplant-050718-100025

Schleissing S., Pfeilmeier S., & Dürnberger C. (2019): **Genome Editing in Agriculture: Between Precaution and Responsibility. An Introduction**
https://www.researchgate.net/profile/Stephan_Schleissing/publication/330917701_Genome_Editing_in_Agriculture_Between_Precaution_and_Responsibility_An_Introduction_Between_Precaution_and_Responsibility/links/5c66997892851c48a9d544c7/Genome-Editing-in-Agriculture-Between-Precaution-and-Responsibility-An-Introduction-Between-Precaution-and-Responsibility.pdf (excellent overview)

Schmidt S.M., Belisle M, Frommer W.B. (2020): **The evolving landscape around genome editing in agriculture** - Many countries have exempted or move to exempt forms of genome editing from GMO regulation of crop plants. EMBO Rep e50680
| https://doi.org/10.15252/embr.202050680
Genome editing is revolutionizing plant science and its applications in agriculture. In its simplest form, it can generate specific genetic variants that are indistinguishable from naturally evolved variants. The legislation and regulation of genome-edited plants in many countries is similarly evolving rapidly to adapt to the new technologies. Here, we summarize and provide an assessment of the current status of this rapidly evolving regulatory landscape, with a focus on recent policy developments in Europe and the global South.
https://www.embopress.org/doi/10.15252/embr.202050680
https://www.embopress.org/doi/epdf/10.15252/embr.202050680

Schulman A.H., Oksman-Caldentey K.-M. and Teeri T.H. (2019): **European Court of Justice delivers no justice to Europe on genome-edited crop.** Plant Biotechnology Journal | https://doi.org/10.1111/pbi.13200
The advent of agriculture about ten millennia ago, the Green Revolution of the 1960s, and all agriculture in-between and since was founded on identification and use of genetic variation. Traditional farmers selected higher producing or better tasting variants and propagated them. The 19th century advent of plant breeding exploited variation by use of sexual crosses. The science of breeding made great progress through the application of Mendelian, quantitative, and population genetics, heterosis, and ultimately molecular markers and genomic selection. However, modern breeders in essence still search for the variation that gives needed traits and introduce it into their breeding programs. The rest is just combining alleles.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/pbi.13200

Seitz C: (2018): **Modifiziert oder nicht? – Regulatorische Rechtsfragen zur Genoptimierung durch neue biotechnologische Verfahren**. EuZW 21, 757 - 764
Am 25.7.2018 hat der EuGH in einem vielbeachteten Grundsatzurteil entschieden, dass durch Mutagenese gewonnene Organismen genetisch veränderte Organismen („GVO“) darstellen und grundsätzlich den in der GVO-Richtlinie vorgesehenen Verpflichtungen unterliegen. Der EuGH stellte fest, dass durch Mutagenese gewonnene Organismen GVO sind, da sie durch die Verfahren und Methoden der Mutagenese eine auf natürliche Weise nicht mögliche Veränderung am genetischen Material eines Organismus vorgenommen wird. Als Ergebnis fallen diese Organismen grundsätzlich in den Anwendungsbereich der GVO-Richtlinie und unterliegen den dort genannten Verpflichtungen. Die GVO-Richtlinie gilt nicht für Organismen aus bestimmten Mutagenese-Verfahren, die herkömmlich in einer Reihe von Anwendungen verwendet wurden und seit Langem als sicher gelten. Im Hinblick auf Organismen, die mit Mutagenese-Verfahren gewonnen werden, die erst nach dem Erlass der GVO-Richtlinie entstanden sind, entschied der EuGH, dass die mit dem Einsatz dieser neuen Mutagenese-Verfahren verbundenen Risiken vergleichbar mit den Risiken aus der Erzeugung und Verbreitung von GVO mittels Transgenese-Verfahren sind. Aufgrund der gemeinsamen Gefahren würde der Ausschluss dieser Organismen aus der GVO-Richtlinie deren Ziel beeinträchtigen, schädliche Auswirkungen auf die menschliche Gesundheit und die Umwelt zu verhindern und würde dem Vorsorgeprinzip widersprechen.

Shao Q., Punt M. and Wesseler J. (2018): **New Plant Breeding Techniques Under Food Security Pressure and Lobbying.** Front. Plant Sci., 19 September 2018
| https://doi.org/10.3389/fpls.2018.01324

Different countries have different regulations for the approval and cultivation of crops developed by using new plant breeding technologies (NPBTs) such as gene editing. In this paper, we investigate the relationship between global food security and the level of NPBT regulation assuming a World Nation Official (WNO) proposes advice on global NPBT food policies. We show that a stricter NPBT food regulation reduces food security as measured by food availability, access, and utilization. We also find that political rivalry among interest groups worsens the food security status, given the NPBT food technology is more productive and the regulatory policy is influenced by lobbying. When the WNO aims to improve food security and weighs the NPBT food lobby contribution more than the non-NPBT food lobby's in the lobbying game, the total lobbying contributions will be the same for the WNO, and the NPBT food lobby will be more successful in the political process. The NPBT food lobby, however, under food security loses its advantage in the political competition, and this may result in a strict NPBT food policy. Under food security problems implementing stricter NPBT food regulations results in welfare losses.
https://www.frontiersin.org/articles/10.3389/fpls.2018.01324/full

Sherkow J.S. (2019): **Controlling CRISPR Through Law: Legal Regimes as Precautionary Principles.** The CRISPR Journal 2 (5) | https://doi.org/10.1089/crispr.2019.0029
Since its advent in 2012, CRISPR has spawned a cottage industry of bioethics literature. One principal criticism of the technology is its virtually instant widespread adoption prior to deliberative bodies conducting a meaningful ethical review of its harms and benefits—a violation, to some, of bioethics' "precautionary principle." This view poorly considers, however, the role that the law can play—and does, in fact, play—in policing the introduction of ethically problematic uses of the technology. This Perspective recounts these legal regimes, including regulatory agencies and premarket approval, tort law and deterrence, patents and ethical licenses, funding agencies and review boards, as well as local politics. Identifying these legal regimes and connecting them to the precautionary principle should be instructive for bioethicists and policy makers who wish to conduct ethical reviews of new applications of CRISPR prior to their introduction.
https://www.liebertpub.com/doi/10.1089/crispr.2019.0029?utm_source=sfmc&utm_medium=email&utm_campaign=CRISPR+FP+Dec+6+2019&d=12%2F6%2F2019&mcid=1501248038&

Shipman, E.N., Yu, J., Zhou, J. et al. (2021): **Can gene editing reduce postharvest waste and loss of fruit, vegetables, and ornamentals?.** *Hortic Res* 8**,** 1 | https://doi.org/10.1038/s41438-020-00428-4
Postharvest waste and loss of horticultural crops exacerbates the agricultural problems facing humankind and will continue to do so in the next decade. Fruits and vegetables provide us with a vast spectrum of healthful nutrients, and along with ornamentals, enrich our lives with a wide array of pleasant sensory experiences. These commodities are, however, highly perishable. Approximately 33% of the produce that is harvested is never consumed since these products naturally have a short shelf-life, which leads to postharvest loss and waste. This loss, however, could be reduced by breeding new crops that retain desirable traits and accrue less damage over the course of long supply chains. New gene-editing tools promise the rapid and inexpensive production of new varieties of crops with enhanced traits more easily than was previously possible. Our aim in this review is to critically evaluate gene editing as a tool to modify the biological pathways that determine fruit, vegetable, and ornamental quality, especially after storage. We provide brief and accessible overviews of both the CRISPR–Cas9 method and the produce supply chain. Next, we survey the literature of the last 30 years, to catalog genes that control or regulate quality or senescence traits that are "ripe" for gene editing. Finally, we discuss barriers to implementing gene editing for postharvest, from the limitations of experimental methods to international policy. We conclude that in spite of the hurdles that remain, gene editing of produce and ornamentals will likely have a measurable impact on reducing postharvest loss and waste in the next 5–10 years.
https://www.nature.com/articles/s41438-020-00428-4

Shukla-Jones A., Friedrich. S., Winickoff D. E. (2018): **Gene editing in an international context Scientific, economic and social issues across sectors.** OECD Science, Technology and Industry Working Papers 2018/04
Gene editing techniques represent a major advance in the field of biotechnological research and application, promising significant benefits across the domains of human health, sustainability and the economy. There is broad agreement that gene editing techniques go beyond incremental advances of past biotechnologies. However, harnessing the potential of gene editing techniques will require meeting significant policy challenges in arenas of governance, ethics, and public engagement. This report summarises the discussions of a group of international experts of science, technology and policy, as well as policymakers at a dedicated workshop entitled "Gene editing in an international context: scientific, economic and social issues across sectors" in Ottawa, Canada on 29-30 September 2016.
https://www.oecd-ilibrary.org/industry-and-services/gene-editing-in-an-international-context_38a54acb-en
https://www.oecd-ilibrary.org/docserver/38a54acb-en.pdf?expires=1565971430&id=id&accname=guest&checksum=6BA50334A48C4C19A43EE0A7FC8FF853

Simionescus L.R., Babeanu N., Cornea C.P. (2019): **Review on legal, social and economic aspects of the new breeding techniques** Scientific Bulletin. Series F. Biotechnologies, Vol. XXIII, 2019I SSN 2285-1364, CD-ROM ISSN 2285-5521, ISSN Online 2285-1372, ISSN-L 2285-1364
The paper aimed to present a review on the social and economic aspects of NBTs, the studies on two different species of plants, subjects of NBT's. The plants variants generated by NBTs are more readily accepted in the market and for crop improvement. In this article we will present briefly the benefits, application and expected developments, regulatory status of NBTs in and outside the EU. It was developed a system for the detection of a

broad spectrum of GMOs for analysis of food/feed matrices by the characterization of transgene flanking regions and the typical combinations for transgene constructs. We will describe two different species of plants, subjects of NBTs: 1) Tomatoes for carotenoid sequestration mechanisms and the carotenoid biosynthesis. The carotenoid accumulation and changes in carotenoid profiles suggest that the plastid can adapt to changes in carotenoid content through plastid differentiation and preferential sequestration; 2) Edited maize genome by biolistic delivery of pre-assembled Cas9-gRNA ribonucleoproteins into maize embryo cells and regeneration of plants with both mutated and edited alleles. As a conclusion, CRISPR/Cas9 is the most used technology for genome editing due to its simplicity and efficiency. In this article, we aim to highlight the application of CRISPR/Cas9 technique system, like the powerful genome editing tool for crop improvement.
http://biotechnologyjournal.usamv.ro/pdf/2019/Art31.pdf

Singer S.D., Laurie J.D., Bilichak A., Kumar S. & Singh J. (2021): **Genetic Variation and Unintended Risk in the Context of Old and New Breeding Techniques.** Critical Reviews in Plant Sciences, | https://doi.org/10.1080/07352689.2021.1883826
For thousands of years, humans have been improving crops to better suit their needs. These enhancements are driven by changes in the genetic makeup of the plant. While this was initially unintentional, there has been a steady push to increase the pace and precision of crop breeding, something that has occurred alongside a growing understanding of genetics and an escalating capacity to thoroughly assess genomes at the molecular level. With the advent and rapid uptake of molecular breeding techniques, such as transgenics and genome editing over the past few decades, there has been much trepidation regarding the possibility of off-target effects derived from unanticipated mutations at loci other than those intended for alteration, and the unintended risks that this might confer. These concerns persist regardless of the fact that a growing number of studies indicate that the occurrence of off-target mutations derived from newer biotechnological breeding techniques are negligible compared to what is observed with many conventional breeding approaches, and even spontaneously from one generation to the next. Given the impending food security crisis that we are facing in the short-term, there is a critical need to implement a wide range of breeding tools as a means of meeting growing demand, withstanding climate change-related pressures, increasing nutrition, and providing environmental benefits. While food safety is clearly of the utmost importance, now is certainly not the time to prevent the use of particular breeding technologies based on unfounded doubts. Therefore, in this review, we attempt to shed light on these apprehensions by putting purported “risks” into the context of plant breeding as a whole by comparing frequencies of spontaneous mutations with those (both anticipated and unanticipated) that occur through various conventional and biotechnological breeding approaches, including transgenics and genome editing. We then consider how these changes may, or may not, translate into unanticipated risk, and discuss the current global regulatory asynchrony surrounding genome edited crops.
https://www.tandfonline.com/doi/full/10.1080/07352689.2021.1883826

Siwo G.H.: (2018): **The Global State of Genome Editing.** Biorxiv: | https://doi.org/10.1101/341198
Genome editing technologies hold great promise in fundamental biomedical research, development of treatments for animal and plant diseases, and engineering biological organisms for food and industrial applications. Therefore, a global understanding of the growth of the field is needed to identify challenges, opportunities and biases that could shape the impact of the technology. To address this, this work applies automated literature mining of scientific publications on genome editing in the past year to infer research trends in 2 key genome editing technologies-CRISPR/Cas systems and TALENs. The study finds that genome editing research is disproportionately distributed between and within countries, with researchers in the US and China accounting for 50% of authors in the field whereas countries across Africa are underrepresented. Furthermore, genome editing research is also disproportionately being explored on diseases such as cancer, Duchene Muscular Dystrophy, sickle cell disease and malaria. Gender biases are also evident in genome editing research with considerably fewer women as principal investigators. The results of this study suggest that automated mining of scientific literature could help identify biases in genome editing research as a means to mitigate future inequalities and tap the full potential of the technology.
https://www.biorxiv.org/content/10.1101/341198v1 Übersicht zu Publikationen

Smedley M.A., Hayta S., Clarke M., Harwood W.A. (2021): **CRISPR-Cas9 Based Genome Editing in Wheat.** Curr Protoc. Mar;1(3) :e65.| doi: 10.1002/cpz1.65
The development and application of high precision genome editing tools such as programmable nucleases are set to revolutionize crop breeding and are already having a major impact on fundamental science. Clustered regularly interspaced short palindromic repeats (CRISPR), and its CRISPR-associated protein (Cas), is a programmable RNA-guided nuclease enabling targeted site-specific double stranded breaks in DNA which, when incorrectly repaired, result in gene knockout. The two most widely cultivated wheat types are the tetraploid durum wheat (Triticum turgidum ssp. durum L.) and the hexaploid bread wheat (Triticum aestivum L.). Both species have large genomes, as a consequence of ancient hybridization events between ancestral progenitors. The highly conserved gene sequence and structure of homoeologs among subgenomes in wheat often permits their simultaneous targeting using CRISPR-Cas9 with single or paired single guide RNA (sgRNA). Since its first successful deployment in wheat, CRISPR-Cas9 technology has been applied to a wide array of gene targets of agronomical and scientific importance. The following protocols describe an experimentally derived strategy for implementing CRISRP-Cas9 genome editing, including sgRNA design, Golden Gate construct assembly, and screening analysis for genome edits. © 2021 The Authors. Basic Protocol 1: Selection of sgRNA target sequence for CRISPR-Cas9 Basic Protocol 2: Construct assembly using Golden Gate (MoClo) assembly Basic Protocol 3:

Screening for CRISPR-Cas9 genome edits Alternate Protocol: BigDye Terminator reactions for screening of CRISPR-Cas9 genome edits.
https://currentprotocols.onlinelibrary.wiley.com/doi/10.1002/cpz1.65
https://currentprotocols.onlinelibrary.wiley.com/doi/epdf/10.1002/cpz1.65

Smyth, S.J., McHughen, A., Entine, J. et al. (2021): **Removing politics from innovations that improve food security.** Transgenic Res | https://doi.org/10.1007/s11248-021-00261-y
Genetically modified (GM) organisms and crops have been a feature of food production for over 30 years. Despite extensive science-based risk assessment, the public and many politicians remain concerned with the genetic manipulation of crops, particularly food crops. Many governments have addressed public concern through biosafety legislation and regulatory frameworks that identify and regulate risks to ensure human health and environmental safety. These domestic regulatory frameworks align to international scientific risk assessment methodologies on a case-by-case basis. Regulatory agencies in 70 countries around the world have conducted in excess of 4400 risk assessments, all reaching the same conclusion: GM crops and foods that have been assessed provide no greater risk to human health or the environment than non-GM crops and foods. Yet, while the science regarding the safety of GM crops and food appears conclusive and societal benefits have been globally demonstrated, the use of innovative products have only contributed minimal improvements to global food security. Regrettably, politically-motivated regulatory barriers are currently being implemented with the next genomic innovation, genome editing, the implications of which are also discussed in this article. A decade of reduced global food insecurity was witnessed from 2005 to 2015, but regrettably, the figure has subsequently risen. Why is this the case? Reasons have been attributed to climate variability, biotic and abiotic stresses, lack of access to innovative technologies and political interference in decision making processes. This commentary highlights how political interference in the regulatory approval process of GM crops is adversely affecting the adoption of innovative, yield enhancing crop varieties, thereby limiting food security opportunities in food insecure economies.
https://link.springer.com/content/pdf/10.1007/s11248-021-00261-y.pdf

Smyth S.J. and Lassoued R. (2018): **Agriculture R&D Implications of the CJEU's Gene-Specific Mutagenesis Ruling.** Trends in Biotechnology, https://doi.org/10.1016/j.tibtech.2018.09.004
On 25 July 2018, the Court of Justice of the European Union (CJEU) ruled that gene-specific mutagenesis must be regulated as genetically modified organism (GMO) technologies. However, the costs to agricultural research and development (R&D) innovation will be staggering, not to mention the brain drain to other countries. As a result, Europe can now be known as the deathplace of agricultural breeding innovations.
https://www.sciencedirect.com/science/article/pii/S0167779918302579

Smyth S.J. (2019) **Global status of the regulation of genome editing technologies**. CAB Rev 14 (21), 1 – 6
Innovations affect societies in various ways. For example, the latest innovations in cell phones and electronics are readily adopted without hesitation. However, many innovations regarding the breeding of plants, the production of food crops and the processing of food products, can be met with fear and trepidation by some societies. Europe, the foundation of the Industrial Revolution, has developed strong adversity to agricultural innovations that involve innovative genome editing methods in general and to genetically modified (GM) crops in particular. While much of the industrial world models their regulatory frameworks for plant agriculture on the science-based risk assessment framework developed through the efforts of the Organisation for Economic Cooperation and Development, the European Union's regulatory framework for GM crops is based on the precautionary principle, approving but a single GM crop variety for production in the twenty-first century. As any field of science and technology advances, so has the breeding of GM crops. GM crop varieties were developed through the insertion of a gene or genes from a different species, such as the insertion of the trait for insect resistance in plants that originally came from a soil bacterium. Crop varieties are now being developed through a group of targeted, site-directed mutation technologies, known as genome editing, where some of this group of technologies results in no foreign genes being transferred into new varieties. While technologically viewed as a significant advancement in the development of new plant varieties, some jurisdictions have chosen to regulate genome editing as equivalent to GM crops, thereby establishing a *de facto* ban on the application of the technology. Yet other jurisdictions have chosen to embrace the technology, announcing that some applications of genome editing will face no regulatory oversight. This paper provides a global overview of the various regulatory frameworks for genome editing.
https://www.cabi.org/cabreviews/review/20193130669

Smyth S.J, Gleim S., Lubieniechi S (2020): **Regulatory barriers to innovative plant breeding in Canada.** Front Genome Ed. https://doi.org/10.3389/fgeed.2020.591592
The regulation of plant breeding is gaining increasing scrutiny, particularly as it pertains to the regulation of gene editing and other new breeding technologies. Genome editing is used worldwide in both public and private plant breeding laboratories and there is considerable uncertainty about the ability of regulatory agencies to match the rapid scientific pace being set. This research focuses on Canada, where advances in plant breeding technology are constrained by the boundaries of the regulatory system established in the early 1990's. This research presents the results of a survey of 93 public and private plant breeders and their views on the existing Canadian regulatory framework regarding conventional breeding and genome editing techniques for plants with novel traits (PNTs). The results contribute to the ongoing debate regarding how, or whether, to regulate

products of genome-edited plant breeding, beyond the existing agronomic and safety requirements. Plant breeders identify the level of Canadian crop research competitiveness and quantify the impacts of novelty within Canada's regulatory system for PNTs. One significant finding is that PNT regulations in Canada have created an innovation barrier in terms of applying genome editing technologies to the development of new varieties, particularly in public sector research.
https://www.frontiersin.org/articles/10.3389/fgeed.2020.591592/full

Smith V., Wesseler J.H.H., Zilberman D. (2021): **New Plant Breeding Technologies: An Assessment of the Political Economy of the Regulatory Environment and Implications for Sustainability.** Sustainability 13, 3687. https://doi.org/10.3390/su13073687
This perspective discusses the impact of political economy on the regulation of modern biotechnology. Modern biotechnology has contributed to sustainable development, but its potential has been underexplored and underutilized. We highlight the importance of the impacts of regulations for investments in modern biotechnology and argue that improvements are possible via international harmonization of approval processes. This development is urgently needed for improving sustainable development. Policy makers in the European Union (EU) in particular are challenged to rethink their approach to regulating modern biotechnology as their decisions have far ranging consequences beyond the boundaries of the EU and they have the power to influence international policies.
https://www.mdpi.com/2071-1050/13/7/3687

The Institute on Science for Global Policy (ISGP) has just released the book "**Sustainable Agriculture: the Role of Plant Breeding Innovation"**, summarizing the outcomes of a conference held on 17-18 November 2020.
https://www.euroseeds.eu/news/new-book-sets-out-plant-breeding-innovations-contribution-to-sustainability/

So D., Sladek R. & Joly J. (2021): **Assessing public opinions on the likelihood and permissibility of gene editing through construal level theory.** New Genetics and Society, DOI: 10.1080/14636778.2020.1868985
Anticipatory policy for gene editing requires assessing public opinion about this new technology. Although previous surveys have examined respondents' views on the moral acceptability of various hypothetical uses of CRISPR, they have not considered whether these scenarios are perceived as plausible. Research in construal level theory indicates that participants make different moral judgments about scenarios seen as likely or near and those seen as unlikely or distant. Therefore, we surveyed a representative sample of 400 Americans and Canadians about both the likelihood and the permissibility of 23 commonly discussed uses of gene editing. Respondents with more knowledge of gene editing generally thought these applications would be more likely within the next 20 years. There was a strong positive relationship between the perceived likelihood and permissibility of most CRISPR applications. Our results suggest that ongoing public engagement efforts for gene editing could be improved by taking its perceived time-frames into account.
https://www.tandfonline.com/doi/abs/10.1080/14636778.2020.1868985?journalCode=cngs20

Somsen H. (2019): S**cientists Edit Genes, Courts Edit Directives. Is the Court of Justice Fighting Uncertain Scientific Risk with Certain Constitutional Risk?** European Journal of Risk Regulation 9(4), 701 – 718 | https://doi.org/10.1017/err.2018.61
https://www.cambridge.org/core/journals/european-journal-of-risk-regulation/article/scientists-edit-genes-courts-edit-directives-is-the-court-of-justice-fighting-uncertain-scientific-risk-with-certain-constitutional-risk/E4A5087303858FDA997337D3AEF7B413

Sowa S., Twardowski T., Woźniak E., Zimny T. (2021): **Legal and practical challenges to authorization of gene edited plants in the EU.** New Biotechnology 60, 183-188 | https://doi.org/10.1016/j.nbt.2020.10.008
According to a predominant interpretation of the C-528/16 judgment of the Court of Justice of the European Union, mutants resulting from gene editing, even those featuring only single nucleotide variants, should be subject to the authorization procedures designed for organisms developed through genetic modification (i.e. insertion of large DNA fragments). In this article, we illustrate practical problems with the authorization of products of gene editing in the EU. On the basis of these problems, we analyze the influence of the current interpretation of EU legislation and judgment on the practical ability to authorize and detect such products on the EU market. We show that the predominant interpretation of the judgment leads to legally unacceptable consequences, in particular to the violation of the principle of proportionality with regard to individuals who wish to develop and market products of gene editing. As a result of our considerations, we show that the C-528/16 judgment did not need to be interpreted in the dominant way.
https://www.sciencedirect.com/science/article/pii/S1871678420301862?via%3Dihub

Spranger T.M. (2018): **Neue Techniken und Europäisches Gentechnikrecht.** NJW 2018, 2929

Sprink, T., Wilhelm, R. A., Spök, A., Robienski, J., Schleissing, S.,Schiemann, J. H., eds. (2020). **Plant Genome Editing – Policies and Governance**. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-88963-670-9 https://www.frontiersin.org/research-topics/7596/plant-genome-editing---policies-and-governance

und in diesem Buch: Schiemann J., Robienski J., Schleissing S., Spök A., Sprink T., Wilhelm R.A. (2020): **Editorial: Plant Genome Editing – Policies and Governance** Front. Plant Sci. | https://doi.org/10.3389/fpls.2020.00284

Stokstad E.:(2021): **Thaw coming for U.K. gene-editing regulations.** *Science* 372 (Issue 6545), 895 |DOI: 10.1126/science.372.6545.895
https://science.sciencemag.org/content/372/6545/895

Sukegawa S., Saika H., Toki S. (2012): **Plant Genome Editing: Ever more precise and wide-reaching.** Plant J. | doi: 10.1111/tpj.15233
Genome editing technologies consisting of targeted mutagenesis and gene targeting enable us to modify genes of interest rapidly and precisely. The discovery in 2012 of CRISPR/Cas9 systems and their development as sequence-specific nucleases has brought about a paradigm shift in biology. Initially, CRISPR/Cas9 was applied in targeted mutagenesis to knock out a target gene. Thereafter, advances in genome editing technologies using CRISPR/Cas9 developed rapidly, with base editing systems for transition substitution using a combination of Cas9 nickase and either cytidine or adenosine deaminase being reported in 2016 and 2017, respectively, and 2021 bringing reports of transversion substitution using Cas9 nickase, cytidine deaminase, and uracil DNA glycosylase. Moreover, technologies for gene targeting and prime editing systems using DNA or RNA as donors have also been developed in recent years. Besides these precise genome editing strategies, reports of successful chromosome engineering using CRISPR/Cas9 have been published recently. The application of genome editing to crop breeding has advanced in parallel with the development of these technologies. Genome editing enzymes can be introduced into plant cells, and there are now many examples of crop breeding using genome editing technologies. At present, it is no exaggeration to say that we are now in a position to be able to modify a gene precisely and rearrange genomes and chromosomes in a predicted way. In this review, we introduce and discuss recent highlights in the field of precise gene editing, chromosome engineering, and genome engineering technology in plants.
Plant J | https://onlinelibrary.wiley.com/doi/10.1111/tpj.15233?af=R

Taffoni G. (2020): **Regulating for Innovation? Insights from the Finnish Presidency of the Council of the European Union.** European Journal of Risk Regulation, 11 , 141–147 | DOI: https://doi.org/10.1017/err.2020.7
https://www.cambridge.org/core/journals/european-journal-of-risk-regulation/article/regulating-for-innovation-insights-from-the-finnish-presidency-of-the-council-of-the-european-union/C3ADE182893AAC8EB16AC0F3A906FDA4

Taning C.N.T., Mezzetti B., Kleter G., Smagghe G., Baraldi E. (2020): **Does RNAi-Based Technology Fit within EU Sustainability Goals?** Trends in Biotechnology |DOI: https://doi.org/10.1016/j.tibtech.2020.11.008
European Union (EU) and global sustainability policies emphasize the need to replace contentious pesticides with safe, efficient, and cost-effective alternatives to ensure sustainable food production. However, R&D for alternatives to contentious pesticides are lagging behind and need to be broadened. Here, we discuss how RNAi-based technology can contribute to pesticide risk reduction.
https://www.cell.com/action/showPdf?pii=S0167-7799%2820%2930303-6

Testbiotech (2020); Kawall K., Miyazaki J., Bauer-Panskus A., Then C. **Overview of genome editing applications using SDN-1 and SDN-2 in regard to EU regulatory issues**
https://www.testbiotech.org/sites/default/files/Overview%20of%20genome%20editing%20applications%20using%20SDN-1%20and%20SDN-2%20in%20regard%20to%20EU%20regulatory%20issues.pdf

Then C. (2018): **Am I Regulated ?**
The US example: why new methods of genetically engineering crop plants need to be regulated
https://www.testbiotech.org/sites/default/files/Am_I_Regulated_en_n.pdf

Thompson P.B. (2020): **Food and Agricultural Biotechnology in Ethical Perspective**
This 3rd edition of Food and Agricultural Biotechnology in Ethical Perspective updates Thompson's analysis to reflect the next generation of biotechnology, including synthetic biology, gene editing and gene drives. The first two editions of this book, published as Food Biotechnology in Ethical Perspective in 1997 and 2007, were the first comprehensive philosophical studies of genetic engineering applied to food systems. The book is structured with chapter length treatments of risk in four categories: food safety, to animals, to the environment and socio-economic risks. These chapters are preceded by two chapters providing orientation to the uses of gene technology in food and agriculture, and to the goals, methods and background assumptions of technological ethics. There is also a chapter covering all four types of risk as applied to the first US technology, recombinant bovine somatotropin. The last four chapters take up 1) intellectual property debates, 2) religious, metaphysical

and “intrinsic” objections to biotechnology, 3) issues in risk and trust and 4) a review of ethical issues in synthetic biology, gene editing and gene drives, the three key technologies that have emerged since the book was last revised.
https://www.springer.com/gp/book/9783030612139

Thygesen P.: **Clarifying the regulation of genome editing in Australia: Situation for genetically modified organisms.** Transgenic Res (2019) 28:151–159 | https://doi.org/10.1007/s11248-019-00151-4
Australia’s gene technology regulatory scheme (GT Scheme) regulates activities with genetically modified organisms (GMOs, organisms modified by gene technology), including environmental releases. The scope of regulation, i.e. what organisms are and are not regulated, is set by the Gene Technology Act 2000 (GT Act) and GT Regulations 2001 (GT Regulations). The GT Act gives broad, overarching definitions of ‘gene technology’ and ‘GMO’ but also provides for exclusions and inclusions in the GT Regulations. Whether organisms developed with genome editing techniques are, or should be, regulated under countries’ national GMO laws is the subject of debate globally. These issues are also under active consideration in Australia. A technical review of the GT Regulations was initiated in 2016 to clarify the regulatory status of genome editing. Proposed draft
amendments are structured around whether the process involves introduction of a nucleic acid template. If agreed, amendments would exclude from regulation organisms produced using site directed nuclease (SDN) 1 techniques while organisms produced using oligonucleotide mutagenesis, SDN-2 or SDN-3 would continue to be regulated as GMOs. The review of the GT Regulations is still ongoing and no legislative changes have been made to the GT Regulations. A broader policy review of the GT Scheme was undertaken in 2017–2018 and as a result further work will be undertaken on the scope and definitions of the GT Act in light of ongoing developments.
https://link.springer.com/article/10.1007%2Fs11248-019-00151-4

transkript: **Grüne Biotechnologie: Sargnagel oder Neubeginn?** Transkript 9, 8-13 (2018)
Der Europäische Gerichtshof hat entschieden: Pflanzen, die mit neuen Verfahren zur zielgerichteten Erbgutveränderung erzeugt wurden, unterliegen künftig der Gentechnik-Richtlinie. Damit schlägt Europa global gesehen einen Sonderweg ein. Pflanzenzüchter, Landwirte und Wissenschaftler sind alarmiert.

Tripathi J.N., Ntui V.O., Shah T., Tripathi L. (2021): **CRISPR/Cas9-mediated editing of *DMR6* Orthologue in banana (*Musa* spp.) confers enhanced resistance to bacterial disease.** Plant Biotechnology Journal | https://doi.org/10.1111/pbi.13614
Banana (*Musa* spp.) is an important staple food crop and a source of income for resource-poor farmers in more than 136 tropical and sub-tropical countries with an annual production of 155 million tons (FAOSTAT, 2018). Many diseases severely constrain banana production, particularly where many pathogens co-exist (Tripathi *et al*., 2020). Banana Xanthomonas wilt (BXW) caused by *Xanthomonas campestris* pv. *musacearum* (Xcm) is considered among the most destructive banana diseases in East and Central Africa (Tripathi *et al*., 2009). All the cultivated banana varieties are susceptible, and only the wild-type progenitor, *Musa balbisiana,* is resistant to BXW disease (Tripathi *et al*., 2019). Overall economic losses from BXW were estimated at US$ 2-8 billion over a decade. The use of disease-resistant varieties is one of the most effective strategies to manage diseases. Recent advances in CRISPR/Cas-based genome-editing can accelerate banana improvement. The availability of reference genome-sequences and the CRISPR/Cas9-editing system has made it possible to develop disease-resistant banana by precisely editing the endogenous genes (Ntui *et al*., 2020).
https://onlinelibrary.wiley.com/doi/epdf/10.1111/pbi.13614 (C-2)

Tsanova T., Stefanova L., Lopalova L, Atanasov A. & Pantchev I. (2021:) **DNA-free gene editing in plants: A brief overview.** Biotechnology &Biotechnological Equipment, 35:1, 131-138, | DOI: 10.1080/13102818.2020.1858159
The conversion of bacterial CRISPR/Cas defense system into a simple and efficient tool for genome manipulations brought experimental biology into new dimensions. Suddenly, genome editing reached many groups most of which were interested in it but not able to employ the available time- and labor-consuming approaches of the pre-CRISPR era. In plant biology and biotechnology, CRISPR/Cas gene editing became the second most important technology after plant transformation. Actually, it relies on the available array of methods of gene delivery. While sufficient for most purposes, the classic gene transfer methods might become a problem for some experimental settings. The main obstacle is that they include DNA delivery and, frequently, its subsequent integration into cellular genome. For this reason novel methods to achieve gene editing without the need of stable transformation and even without DNA delivery were developed. These new approaches include *in vitro* ribonucleoprotein complexes formulations (delivered by microinjection, particle bombardment, electroporation, liposomes etc.), use of virus-like particles and employment of bacterial secretory systems for Cas/gRNA delivery. The first attempts to achieve DNA-free editing were made less than ten years ago. Later, different types of animal and plant cells were addressed. In this mini review we try to summarize the current developments and emerging trends in the field of DNA-free editing in plants.
https://www.tandfonline.com/doi/pdf/10.1080/13102818.2020.1858159?needAccess=true

Tsuda M., Watanabe K.N., Ohsawa R. (2019): **Regulatory Status of Genome-Edited Organisms Under the Japanese Cartagena Act.** Front. Bioeng. Biotechnol., 06 December 2019 | https://doi.org/10.3389/fbioe.2019.00387

The Japanese government recognizes the substantial values of genome-edited agricultural organisms and has defined in which cases these are covered by the existing regulatory framework to handle this technology. Genome-editing technologies could revolutionize and accelerate plant breeding owing to the simplicity of the methods and precision of genome modifications. These technologies have spread rapidly and widely, and various genome-edited crops have been developed recently. The regulatory status of genome-edited end products is a subject of controversy worldwide. In February 2019, the Japanese government defined genome-edited end products derived by modifications of SDN-1 type (directed mutation without using a DNA sequence template) as not representing "living modified organisms" according to the Japanese Cartagena Act. Here, we describe the classification and regulatory status of genome-edited end products in this decision. We hope that reporting the progress in Japan toward the implementation of this regulatory approach will provide insight for scientific and regulatory communities worldwide.
https://www.frontiersin.org/articles/10.3389/fbioe.2019.00387/full

Turnbull C., Lillemo M., Hvoslef-Eide T.A.K. (2021): **Global Regulation of Genetically Modified Crops Amid the Gene Edited Crop Boom - A Review.** Front. Plant Sci. | https://doi.org/10.3389/fpls.2021.630396
Products derived from agricultural biotechnology is fast becoming one of the biggest agricultural trade commodities globally, clothing us, feeding our livestock, and fueling our eco-friendly cars. This exponential growth occurs despite asynchronous regulatory schemes around the world, ranging from moratoriums and prohibitions on genetically modified (GM) organisms, to regulations that treat both conventional and biotech novel plant products under the same regulatory framework. Given the enormous surface area being cultivated, there is no longer a question of acceptance or outright need for biotech crop varieties. Recent recognition of the researchers for the development of a genome editing technique using CRISPR/Cas9 by the Nobel Prize committee is another step closer to developing and cultivating new varieties of agricultural crops. By employing precise, efficient, yet affordable genome editing techniques, new genome edited crops are entering country regulatory schemes for commercialization. Countries which currently dominate in cultivating and exporting GM crops are quickly recognizing different types of gene-edited products by comparing the products to conventionally bred varieties. This nuanced legislative development, first implemented in Argentina, and soon followed by many, shows considerable shifts in the landscape of agricultural biotechnology products. The evolution of the law on gene edited crops demonstrates that the law is not static and must adjust to the *mores* of society, informed by the experiences of 25 years of cultivation and regulation of GM crops. The crux of this review is a consolidation of the global legislative landscape on GM crops, as it stands, building on earlier works by specifically addressing how gene edited crops will fit into the existing frameworks. This work is the first of its kind to synthesize the applicable regulatory documents across the globe, with a focus on GM crop cultivation, and provides links to original legislation on GM and gene edited crops.
https://www.frontiersin.org/articles/10.3389/fpls.2021.630396/full

USDA-APHIS**: Revisions to USDA-APHIS 7 CFR part 340 Regulations Governing the Movement of Organisms Modified or Produced Through Genetic Engineering**
https://www.aphis.usda.gov/biotechnology/340-secure-rule-eis.pdf

https://www.aphis.usda.gov/biotechnology/340-secure-rule.pdf

https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/secure-rule/secure-about/340_2017_perdue_biotechreg

UDSA: **NATIONAL ENVIRONMENTAL POLICY ACT -** PRELIMINARY FINDING OF NO SIGNIFICANT IMPACT Regarding Deregulating a Petition (19-099-01p) Under 7 CFR part 340 from: Westhoff Vertriebsgesellschaft mbH A1-DFR petunias
https://www.aphis.usda.gov/brs/aphisdocs/19_09901p_pfonsi.pdf

Urnov F.D., Ronold P.C. and Carrol D. (2018): **A call for science-based review of the European court's decision on gene-edited crops**. Nature Biotechnology 36, 800-802
https://www.nature.com/articles/nbt.4252

VAN DER MEER P., ANGENON G., BERGMANS H., BUHK H.J. et al. (2021): **The Status under EU Law of Organisms Developed through Novel Genomic Techniques.** European Journal of Risk Regulation (2020), page 1 of 20 doi:10.1017/err.2020.105
In a ruling on 25 July 2018, the Court of Justice of the European Union concluded that organisms obtained by means of techniques/methods of mutagenesis constitute GMOs in the sense of Directive 2001/18, and that organisms obtained by means of techniques/methods of directed mutagenesis are not excluded from the scope of the Directive. Following the ruling, there has been much debate about the possible wider implications of the ruling. In October 2019, the Council of the European Union requested the European Commission to submit, in light of the CJEU ruling, a study regarding the status of novel genomic techniques under Union Law. For the purpose of the study, the Commission initiated stakeholder consultations early in 2020. Those consultations focused on the technical status of novel genomic techniques.

This article aims to contribute to the discussion on the legal status of organisms developed through novel genomic techniques, by offering some historical background to the negotiations on the European Union (EU) GMO Directives as well as a technical context to some of the terms in the Directive, and by analysing the ruling. The article advances that (i) the conclusion that organisms obtained by means of techniques/methods of mutagenesis constitute GMOs under the Directive means that the resulting organisms must comply with the GMO definition, ie the genetic material of the resulting organisms has been altered in a way that does not occur naturally by mating and/or natural recombination; (ii) the conclusion that organisms obtained by means of techniques/methods of directed mutagenesis were not intended to be excluded from the scope of the Directive is not inconsistent with the negotiation history of the Directive; (iii) whether an organism falls under the description of "obtained by means of techniques/methods of directed mutagenesis" depends on whether the genetic material of the resulting organisms has been altered in a way that does not occur naturally by mating and/or natural recombination. Finally, the article offers an analysis of the EU GMO definition, concluding that for an organism to be a GMO in the sense of the Directive, the technique used, as well as the genetic alterations of the resulting organism, must be considered.
https://www.cambridge.org/core/journals/european-journal-of-risk-regulation/article/status-under-eu-law-of-organisms-developed-through-novel-genomic-techniques/4812A77647B94B3BB789D3532379C081

Van Eenennaam A.L., Wells K.D. & Murray J.D, (2019): **Proposed U.S. regulation of gene-edited food animals is not fit for purpose.** *npj Science of Food* 3, Article number:3
Dietary DNA is generally regarded as safe to consume, and is a routine ingredient of food obtained from any living organism. Millions of naturally-occurring DNA variations are observed when comparing the genomic sequence of any two healthy individuals of a given species. Breeders routinely select desired traits resulting from this DNA variation to develop new cultivars and varieties of food plants and animals. Regulatory agencies do not evaluate these new varieties prior to commercial release. Gene editing tools now allow plant and animal breeders to precisely introduce useful genetic variation into agricultural breeding programs. The U.S. Department of Agriculture (USDA) announced that it has no plans to place additional regulations on gene-edited plants that could otherwise have been developed through traditional breeding prior to commercialization. However, the U.S. Food and Drug Administration (FDA) has proposed mandatory premarket new animal drug regulatory evaluation for all food animals whose genomes have been intentionally altered using modern molecular technologies including gene editing technologies. This runs counter to U.S. biotechnology policy that regulatory oversight should be triggered by unreasonable risk, and not by the fact that an organism has been modified by a particular process or technique. Breeder intention is not associated with product risk. Harmonizing the regulations associated with gene editing in food species is imperative to allow both plant and animal breeders access to gene editing tools to introduce useful sustainability traits like disease resistance, climate adaptability, and food quality attributes into U.S. agricultural breeding programs.
https://www.nature.com/articles/s41538-019-0035-y
https://www.nature.com/articles/s41538-019-0035-y.pdf

Van Eenennaam A.L:, De Figueiredo Silva F. Trott J.F. Zilberman FD.(2021) **Genetic Engineering of Livestock: The Opportunity Cost of Regulatory Delay.** Annual Review of Animal Biosciences, 9:1
Genetically engineered (GE) livestock were first reported in 1985, and yet only a single GE food animal, the fast-growing AquAdvantage salmon, has been commercialized. There are myriad interconnected reasons for the slow progress in this once-promising field, including technical issues, the structure of livestock industries, lack of public research funding and investment, regulatory obstacles, and concern about public opinion. This review focuses on GE livestock that have been produced and documents the difficulties that researchers and developers have encountered en route. Additionally, the costs associated with delayed commercialization of GE livestock were modeled using three case studies: GE mastitis-resistant dairy cattle, genome-edited porcine reproductive and respiratory syndrome virus–resistant pigs, and the AquAdvantage salmon. Delays of 5 or 10 years in the commercialization of GE livestock beyond the normative 10-year GE product evaluation period were associated with billions of dollars in opportunity costs and reduced global food security.
Expected final online publication date for the *Annual Review of Animal Biosciences*, Volume 9 is February 16, 2021.
Please see http://www.annualreviews.org/page/journal/pubdates for revised estimates.
https://www.annualreviews.org/doi/10.1146/annurev-animal-061220-023052

van Harmelen J. (2019): **New breeding techniques and regulation of genetically modified organisms**
Regulation Südafrika – EuGH-Urteil
https://www.lexology.com/library/detail.aspx?g=6d15b78f-e62b-4ea9-89c4-c9175f18279a

Van Montagu M.: (2019): **The future of plant biotechnology in a globalized and environmentally endangered world.** Genet. Mol. Biol.43 (1 supl.2 Ribeirão Preto2020 Epub Dec 20, 2019
http://dx.doi.org/10.1590/1678-4685-gmb-2019-0070
This paper draws on the importance of science-based agriculture in order to throw light on the way scientific achievements are at the basis of modern civilization. An overview of literature on plant biotechnology innovations and the need to steer agriculture towards sustainability introduces a series of perspectives on how plant biotech can contribute to the major challenge of feeding our super population with enough nutritious food without further compromise of the environment. The paper argues that science alone will not solve problems. Three

major forces - science, the economy and society - shape our modern world. There is a need for a new social contract to harmonize these forces. The deployment of the technologies must be done on the basis of ethical and moral values.

Vives-Vallés J.A. and Collonnier C. (2020): **The Judgment of the CJEU of 25 July 2018 on Mutagenesis: Interpretation and Interim Legislative Proposal**. Front. Plant Sci., 03 March 2020 | https://doi.org/10.3389/fpls.2019.01813

The Judgment of 25 July 2018 of the Court of Justice of the European Union (CJEU)[1] was optimistically awaited by breeders and supporters of agricultural biotechnology, but shortly after the press release advancing the Judgment, hope turned into frustration. Opinions on how to frame the New Breeding Techniques (NBT) in the context of Directive 2001/18/EC were issued before the Judgment, while proposals to assist the EU legislator to amend the regime driven by the Directive have been also provided afterwards by scientists and institutional bodies around the EU. However, they do not seem to have paid so much attention to the Judgment itself. This paper focuses on the Judgment. It finds out that while the impacts of the Judgment on the NBT might have been slightly overvalued, its potential negative effects on techniques of random mutagenesis and varieties breed through them have been generally underestimated if not absolutely overlooked. The analysis also shows that the Judgment does not preempt the possibility to exempt certain applications of some NBT from the scope of Directive 2001/18/EC,[2] and, in fact, ODM, SDN1, and SDN2 might be, under certain conditions, easily exempted from its scope without the need of a deep legislative revolution nor even the amendment of Directive 2001/18/EC. As regards techniques of random mutagenesis and mutant varieties bred by means of those techniques, until action is taken by Member States (if finally taken), no real limitations upon them are to be feared. However, if Member States start to consider the path opened by the CJEU, then their regulation at an EU level should be readily explored in order to avoid further negative effects on plant breeding as well as on the free movement inside the EU of those varieties and the products thereof.
https://www.frontiersin.org/articles/10.3389/fpls.2019.01813/full

Voigt: **Anmerkung zum EuGH-Urteil „Mutagenese“** ZLR 5/2018, 654

Gerichtshof der Europäischen Union – “Mutagenese” ZLR 5/2018,637

Volling A. im Auftrag von Maria Heubuch, MdEP Mai 2019: **Keine Gentechnik durch die Hintertür**

Nach dem EuGH-Urteil vom 25. Juli 2018 hat die Diskussion um die neuen Gentechnik-Verfahren noch mal an Schärfe gewonnen. Nachdem zunächst das EuGH-Urteil von interessierten Kreisen als „nicht wissenschaftlich“, „rückwärtsgewandt“ und „innovationsfeindlich“ dargestellt wurde, nimmt der Druck auf die Politik zu, die Gentechnik-Richtlinie 2001/18 zu ändern oder zu öffnen. In der vorliegenden Studie wird einleitend das EuGH-Urteil vom 25. Juli 2018 dargestellt und bewertet. Da-nach werden zum Überblick einige Positions- und Forderungspapiere der Gentechnik-Befürworter*innen aufgeführt, die mit einigem zeitlichen Abstand zum Urteil veröffentlicht wurden und die in die Richtung plädieren, die Gentechnik-Richtlinie zu ändern. Im Oktober 2018 veröffentlichten Forscher von wissenschaftlichen Institutionen und Universitäten einen öffentlichen Brief. Darauf folgte der „Bioökonomierat“, der sich als Beratungsgremium der Bundesregierung versteht. Im Frühjahr 2019 zogen die Agrarindustrie-Verbände nach, erst aus Deutschland, dann die europäischen Dachverbände, die entsprechende Forde-rungen vorbringen. Zudem werden die Äußerungen von einzelnen WTO-Ländern, der EU-Kommission und der deutschen Bundesregierung dargestellt. Die Argumente und Forderungen werden jeweils geclustert und dann einer ausführlichen Prüfung und Bewertung unterzogen. Abschließend wird erläutert, warum wir eine Regulierung zum Erhalt einer gentech-nikfreien Züchtung, Landwirtschaft und Lebensmittelerzeugung brauchen.
https://www.maria-heubuch.eu/fileadmin/heubuch/pdf2019/Heubuch_Warum_eine_Regulierung_der_neuen_Gentechnik_notwendig_ist_28.05.2019_fertig.pdf

Wanner B., Monconduit H., Mertens A., Thomaier J. (2019): **CJEU renders decision on the interpretation of the GMO Directive** *Journal of Intellectual Property Law & Practice*, Volume 14, Issue 2, 1 February 2019, Pages 90–92, https://doi.org/10.1093/jiplp/jpy184
https://academic.oup.com/jiplp/article-abstract/14/2/90/5288297?redirectedFrom=fulltext

Wasmer M. S.: **Roads Forward for European GMO Policy – Uncertainties in Wake of ECJ Judgment Have to be Mitigated by Regulatory Reform.** Front. Bioeng. Biotechnol.
| doi: 10.3389/fbioe.2019.00132

This article gives an overview of legal and procedural uncertainties regarding genome edited organisms and possible ways forward for European GMO policy. After a recent judgment by the European Court of Justice (ECJ judgment of 25 July 2018, C-528/16), organisms obtained by techniques of genome editing are GMOs and subject to the same obligations as transgenic organisms. Uncertainties emerge if genome edited organisms cannot be distinguished from organisms bred by conventional techniques, such as crossing or random mutagenesis. In this case, identical organisms can be subject to either GMO law or exempt from regulation because of the use of a technique that cannot be identified. Regulatory agencies might not be able to enforce GMO law for such cases in the long term. As other jurisdictions do not regulate such organisms as GMOs, accidental imports might occur and undermine European GMO regulation. In the near future, the EU Commission as well as European and national regulatory agencies will decide on how to apply the updated interpretation of the law. In order to mitigate

current legal and procedural uncertainties, a first step forward lies in updating all guidance documents to specifically address genome editing and allowing a differentiated assessment for different types of GMOs. Especially organisms bred by new echniques and whose traits do not pose any known risks should benefit from a more dynamic and predictable authorization procedure for GMO release, including a solution for providing a unique identifier. In part, this can be achieved by making use of existing flexibilities in GMO law. However, only an amendment to the regulations that govern the process of authorization for GMO release can substantially lower the burden for innovators. In a second step, any way forward has to aim at amending, supplementing or replacing the European GMO Directive (2001/18/EC).The policy options presented in this article presuppose political readiness for reform. This may not be realistic in the current political situation. However, if the problems of current GMO law are just ignored, European competitiveness and research in green biotechnology will suffer.
https://www.frontiersin.org/articles/10.3389/fbioe.2019.00132/abstract

Wesseler J., Politiek H. and Zilberman D. (2019): **The Economics of Regulating New Plant Breeding Technologies - Implications for the Bioeconomy Illustrated by a Survey Among Dutch Plant Breeders.** Front. Plant Sci. 10:1597. | https://doi.org/10.3389/fpls.2019.01597
New plant breeding technologies (NPBTs) are increasingly used for developing new plants with novel traits. The science tells us that those plants in general are as safe as than those once developed using "conventional" plant breeding methods. The knowledge about the induced changes and properties of the new plants by using NPBTs is more precise. This should lead to the conclusion that plants developed using NPBTs should not be regulated differently than those developed using "conventional" plant breeding methods. This contribution discusses the economics of regulating new plant breeding technologies. We first develop the theoretical model and elaborate on the different regulatory approaches being used and compare their advantages and disadvantages. Then we provide a perspectives on EU regulation around mutagenesis-based New Plant Breeding Techniques (NPBT), formed by new insights from a survey among Dutch plant breeding companies. The survey measures the attitude of breeding companies towards the ruling of the EU Court of Justice that subjected the use of CRISPR-Cas in the development of new plant varieties under the general EU regulations around GMOs. The results show that plant breeders experience a financial barrier because of the ruling, with perceived negative impact on competitiveness and investments in CRISPR-Cas as a result. The degree of negative impact differs however significantly among seed-sectors and company sizes. One of the most striking results was the relative optimism of companies in the sector about more lenient legislation in the next five years, despite the stated negative effects.
https://www.frontiersin.org/articles/10.3389/fpls.2019.01597/full

Whelan A. I., Gutti P. and Martin A. Lema M.A. (2020): **Gene Editing Regulation and Innovation Economics.** Front. Bioeng. Biotechnol., 15 April 2020 |
https://doi.org/10.3389/fbioe.2020.00303
Argentina was the first country that enacted regulatory criteria to assess if organisms resulting from new breeding techniques (NBTs) are to be regarded as genetically modified organisms (GMOs) or not. The country has now accumulated 4 year of experience applying such criteria, reaching a considerable number of cases, composed mostly of gene-edited plants, animals, and microorganisms of agricultural use. This article explores the effects on economic innovation of such regulatory experience. This is done by comparing the cases of products derived from gene editing and other NBTs that have been presented to the regulatory system, against the cases of GMOs that have been deregulated in the country. Albeit preliminary, this analysis suggests that products from gene editing will have different profiles and market release rates compared with the first wave of products from the so called "modern biotechnology." Gene editing products seems to follow a much faster development rate from bench to market. Such development is driven by a more diverse group of developers, and led mostly by small and medium enterprises (SMEs) and public research institutions. In addition, product profiles are also more diversified in terms of traits and organisms. The inferences of these findings for the agricultural and biotechnology sectors, particularly in developing countries, are discussed.
https://www.frontiersin.org/articles/10.3389/fbioe.2020.00303/full

Wight A.J. (2018): **Strict EU ruling on gene-edited crops squeezes science**
Researchers are feeling the pinch and demanding exemptions for plant science and agriculture.
https://www.nature.com/articles/d41586-018-07166-7

Winter G.: (2020): **Neue Gentechniken und Naturschutz als Regulierungsproblem.** Natur und Landschaft 95 (5), 226-234 |DOI 10.17433/5.2020.50153805.226-234
Neue Gentechniken bieten Chancen für neue Ziele nachhaltigen Wirtschaftens, verursachen aber auch neue Risiken für Mensch und Umwelt. Dies gilt im Besonderen für solche Anwendungen der neuen Gentechniken, die dem Naturschutz dienen sollen. Damit stellt sich die Frage, ob das geltende Recht der Biotechnologie den Entwicklungen hinreichend Rechnung trägt. Der folgende Beitrag beginnt mit einer Strukturierung der neuen Gentechniken in regulatorischer Perspektive und untersucht dann, ob sich Änderungen im Anwendungsbereich, in den Instrumenten, in den Bewertungsmethoden und in den materiellen Kriterien der Regulierung empfehlen. Der Schwerpunkt liegt dabei darauf, wie das Gentechnikrecht - insbesondere unter Naturschutzaspekten - anzupassen ist. Zugleich wird aber auch untersucht, ob die gentechnikbezogenen Normen des Naturschutzrechts änderungsbedürftig sind.
https://www.natur-und-landschaft.de/de/news/neue-gentechniken-und-naturschutz-als-regulierungsproblem-1434

Winter G. (2021): **Regulierungsfragen angesichts Neuer Gentechniken** - Wie weiter nach dem Urteil des Europäischen Gerichtshofes?
In: ABL: CRISPR/Cas **Neue Gentechnik Regulierung oder Freifahrtschein?** Texte zur aktuellen Diskussion
http://abl-ev.de/fileadmin/Dokumente/AbL_ev/Publikationen/AbL_CRISPR___CO_Neue_Gentechnik_-_Regulierung_oder_Freifahrtschein_WEB6_vorab.pdf

Wolt J. and Wolf C. (2019): **Policy and Governance Perspectives for Regulation of Genome Edited Crops in the United States.** Front. Plant Sci., 08 November 2018 | https://doi.org/10.3389/fpls.2018.01606
Genome editing for crop improvement lies at the leading edge of disruptive bioengineering technologies that will challenge existing regulatory paradigms for products of biotechnology and which will elicit widespread public interest. Regulation of products of biotechnology through the US Coordinated Framework for Biotechnology is predicated on requiring burden of proof that regulation is warranted. Although driven by considerations of newly emerging processes for product development, regulation has, for the most part, focused on characteristics of the biotechnology product itself and not the process used for its development *per se*. This standard of evidence and product focus has been maintained to date in regulatory considerations of genome edited crops. Those genome edited crops lacking recombinant DNA (rDNA) in the product intended for environmental release, lacking plant pest or pesticidal activity, or showing no food safety attributes different from those of traditionally bred crops are not deemed subject to regulatory evaluation. Regardless, societal uncertainties regarding genome editing are leading regulators to seek ways whereby these uncertainties may be addressed through redefinition of those products of biotechnology that may be subject to regulatory assessments. Within US law prior statutory history, language and regulatory action have significant influence on decision making; therefore, the administrative law and jurisprudence underlying the current Coordinated Framework strongly inform policy and governance when considering new plant breeding technologies such as genome editing.
https://www.frontiersin.org/articles/10.3389/fpls.2018.01606/full

Zakaria H. (2020). **Drivers of the various stands on the debate on GM crops: What are the real motives beyond the public rhetoric?** GSC Advanced Research and Reviews, 2(3), 09-17 | https://doi.org/10.30574/gscarr.2020.2.3.0009
The underlying constructs characterising the never-ending debate and lack of consensus on food are largely issues relating to potential risks and uncertainty GMOs might pose to human health and the environment, and the possible threats to national food sovereignty. This paper is a review study and as such relied solely on published literature on contentious issues surrounding GM crops and its food derivatives. Most of the issues raised in available literature against GMOs on the grounds of health and environmental risks, and national food sovereignty concerns are overhyped, speculative and fear-mongering. Public interest and safety will be better assured and safeguarded if GMOs proponents and opponents reached consensus on standardization regarding tolerable level of harm and acceptable safety limit in interpreting impact assessment results of GMOs on health and environment.
https://gsconlinepress.com/journals/gscarr/content/drivers-various-stands-debate-gm-crops-what-are-real-motives-beyond-public-rhetoric

Zhang D., Hussain A., Manghwar H., Xie K. et al. (2020**): Genome editing with the CRISPR-Cas system: an art, ethics and global regulatory perspective.** Plant Biotechnology Journal 18, 1651–1669 | https://doi.org/10.1111/pbi.13383
Over the last three decades, the development of new genome editing techniques, such as ODM, TALENs, ZFNs and the CRISPR-Cas system, has led to significant progress in the field of plant and animal breeding. The CRISPR-Cas system is the most versatile genome editing tool discovered in the history of molecular biology because it can be used to alter diverse genomes (e.g. genomes from both plants and animals) including human genomes with unprecedented ease, accuracy and high efficiency. The recent development and scope of CRISPR-Cas system have raised new regulatory challenges around the world due to moral, ethical, safety and technical concerns associated with its applications in pre-clinical and clinical research, biomedicine and agriculture. Here, we review the art, applications and potential risks of CRISPR-Cas system in genome editing. We also highlight the patent and ethical issues of this technology along with regulatory frameworks established by various nations to regulate CRISPR-Cas-modified organisms/products.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/pbi.13383

Zimny T., Sowa S., Tyczewska A., Twardowski T.: (2019): **Certain new plant breeding techniques and their marketability in the context of EU GMO legislation – recent developments.** New Biotechnology 51, 49-56 | https://doi.org/10.1016/j.nbt.2019.02.003
The comparatively low adoption rate of GMO products in the European Union (EU) market seems to be connected with the strictness of authorization regulations and inefficiency of the authorization process itself. These problems will apply to any product deemed to be a GMO that could potentially be marketable in the EU. Since modern methods of plant breeding involving oligonucleotide-directed mutagenesis (ODMs) or site-directed nucleases (SDNs), including Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), are becoming ever more popular, it is crucial to establish whether the products of such new breeding techniques (NBTs), in particular those which involve precise methods of mutagenesis, are exempted from the EU legislation on GMOs or not. Legal uncertainty as to their status may result in reluctance to invest in such methods and develop them further.

Here, developments are presented in the legal classification of certain NBTs products in the context of recent decisions and jurisprudence. The socioeconomic aspects of GMO adoption in both global and European contexts are discussed. The legal and practical landscape of GMO regulation in the EU is presented and how it may pose an obstacle to investment and the development of new products. The latest jurisprudence (e.g., Case C-528/16) [1] on the interpretation of the legal concept of GMOs and the scope of the legislation are analyzed, with the conclusion that the strict regulations will probably also apply to products of the NBTs involving precise methods of mutagenesis. This in turn will probably result in the restriction of their application in the development of new plant varieties in the EU.
https://www.sciencedirect.com/science/article/pii/S187167841831940X

Zimmy T. and Eriksson D. (2020): **Exclusion or exemption from risk regulation?**
A comparative analysis of proposals to amend the EU GMO legislation
EMBO Rep (2020)e51061 | https://doi.org/10.15252/embr.202051061
In the EU, the legal status of agricultural products resulting from the use of new breeding techniques (NBTs)—among others the new gene-editing technologies—has been subject to dispute even before the Court of Justice of the EU (CJEU) ruled that products of newer forms of mutagenesis should be regulated as genetically modified organisms (GMOs; Breyer *et al*, 2009; Abbott, 2015). In November 2019, the Council of the EU requested the European Commission (EC) to submit a study, and a proposal if appropriate, for addressing the legal status of novel genomic techniques under Union law, and this will likely provide more clarity for the products of NBTs. In the meantime, several proposals for amending the current GMO legislation have been published. We here provide an analysis of their respective key features, similarities and differences, and potential implications of their adoption.
https://www.embopress.org/doi/full/10.15252/embr.202051061

Zhan X., Lu Y., Zhu J.-K., Botella J.R. (2020): **Genome editing for plant research and crop improvement.** JIPB | https://doi.org/10.1111/jipb.13063
The advent of CRISPR has had a profound impact on plant biology, and crop improvement. In this review, we summarize the state-of-the-art development of CRISPR technologies and their applications in plants, from the initial introduction of random small indel (insertion or deletion) mutations at target genomic loci to precision editing such as base editing, prime editing and gene targeting. We describe advances in the use of class 2, types II, V and VI systems for gene disruption as well as for precise sequence alterations, gene transcription and epigenome control.
https://onlinelibrary.wiley.com/doi/epdf/10.1111/jipb.13063