Utilisation of New Genome Editing Techniques in Finland

Nina Wessberg, Santtu Lehtinen, Anneli Ritala, Suvi T. Häkkinen, VTT
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Abstract

The objective of this report is to produce information on the current state and future of the new genome editing techniques. The report material was collected from the literature, supported by expert interviews and business surveys. In addition, two stakeholder meetings were organised. Furthermore, statistics and the scenario method were utilised in the project.

The new genome editing techniques enable one to add, remove or edit the desired qualities of an organism very accurately and in a targeted way. In Finland, these techniques are mainly applied in basic research on plants and in animal physiology, as well as in medical research and development to produce test animal and cell models.

Genome editing techniques could be applied for improving the climate resilience of plants as growing conditions become altered by climate change. In addition to medical trials, the techniques enable development of gene therapeutic treatments. In animal breeding, the expectations centre on improving health and wellbeing of animals.

The development of applications is hindered by the interpretation of European legislation that equates the new genome editing techniques with genetic modification. This keeps the costs of the required risk evaluation high. In addition, the consumer stance towards gene modification is negative, which means that the market of genome edited products is viewed as unstable.

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Keywords research, research activities, CRISPR-Cas9, genome editing, gene editing, scenario

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Kuvailulehti
21.5.2021

Uusien genominmuokkaustekniikoiden hyödyntäminen Suomessa

Valtioneuvoston selvitys- ja tutkimustoiminnan julkaisusarja 2021:39

Julkaisija	Valtioneuvoston kanslia		
Tekijä/t	Nina Wessberg, Santtu Lehtinen, Anneli Ritala, Suvi T. Häkkinen, Johanna Vilkki, Alan Schulman, Jussi Laine, Satu Korhonen		
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Tiivistelmä

Tämän selvityksen tarkoitus on tuottaa tietoa uusien genominmuokkaustekniikoiden nykytilasta ja tulevaisuudesta. Selvityksen aineisto kerättiin kirjallisuudesta, asiantuntijahaastatteluin sekä yrityskyselyn avulla. Hankkeessa järjestettiin kaksi sidosryhmätilaisuutta. Lisäksi hyödynnettiin tilastoaineistoa ja skenaariomenetelmää.

Uusilla genominmuokkaustekniikoilla on mahdollista lisätä, poistaa tai muokata organismin haluttuja ominaisuuksia hyvin tarkasti ja kohdennetusti. Niitä sovelletaan tällä hetkellä Suomessa pääasiassa kasvintutkimuksen ja eläinfysiologian perustutkimuksessa sekä lääketieteellisessä tutkimuksessa ja kehityksessä tuottamalla geenieditoinnilla koe-eläin- ja solumalleja.

Uusia genominmuokkaustekniikoita voitaisiin soveltaa mm.kasvien säänkestävyyden parantamiseen ilmastonmuutoksen muuttamissa kasvuolosuhteissa. Lääketieteessä lääketutkimuksen lisäksi uudet genominmuokkaustekniikat mahdollistavat geeniterapeuttisten hoitojen kehittämisen. Eläinjalostuksessa toiveet kohdistuvat eläinten terveyden hyvinvoinnin parantamiseen.

Sovellusten tuottamisen kasvua estävät eurooppalainen lainsäädännön tulkinta, joka rinnastaa uudet genominmuokkaustekniikat geenimuunteluun. Tämä pitää vaaditun riskinarvioinnin kustannukset korkeina. Lisäksi kuluttajien asenne geenimuuntelua kohtaan on negatiivinen, jolloin myös genominmuokattujen tuotteiden markkinat koeteen epävarmoiksi.

Klausuuli Tämä julkaisu on toteutettu osana valtioneuvoston selvitys- ja tutkimussuunnitelman toimeenpanoa. (tietokayttoon.fi) Julkaisun sisällöstä vastaavat tiedon tuottajat, eikä tekstisisältö välttämättä edusta valtioneuvoston näkemystä.

Asiasanat tutkimus, tutkimustoiminta, CRISPR-Cas9, genominmuokkaus, geenieditointi, skenaario

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Nyttjandet av nya genomredigeringstekniker i Finland

Publikationsserie för statsrådets utrednings- och forskningsverksamhet 2021:39

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Författare	Nina Wessberg, Santtu Lehtinen, Anneli Ritala, Suvi T. Häkkinen, Johanna Vilkki, Alan Schulman, Jussi Laine, Satu Korhonen		
Utarbetad av	VTT, LUKE, Demos Helsinki		
Språk	engelska	**Sidantal**	98

Referat

Syftet med utredningen är att producera information om nuläget och framtiden för nya genomredigeringstekniker. Materialet samlades in från litteraturen, genom intervjuer med experter och med en företagsundersökning. I projektet ordnades två möten för intressenter. Dessutom användes statistiskt material och scenariometoden.

Med nya genomredigeringstekniker kan man göra riktade förändringar med hög precision hos en organism genom att lägga till, ta bort eller förändra specifika egenskaper hos organismen. I Finland tillämpas teknikerna främst inom växtforskning, grundforskning i djurfysiologi samt medicinsk forskning och utveckling där man producerar försöksdjurs- och cellmodeller genom geneditering.

Nya genomredigeringstekniker skulle kunna användas bland annat för att anpassa växter till de nya förhållandena som klimatförändringen medför. Inom den medicinska sektorn skapar teknikerna möjligheter för läkemedelsprövning och potential att utveckla genterapeutiska behandlingar. Inom husdjursaveln är målen inställda på att förbättra djurhälsan.

Produktionen av tillämpningar fördröjs av tolkningen av den europeiska lagstiftningen, som jämställer nya genomredigeringstekniker med genmodifiering. Tolkningen innebär höga kostnader för riskbedömning. Dessutom har konsumenterna en negativ inställning till genmodifiering och därför anses marknaden för genomredigerade produkter osäker.

Nyckelord	forskning, forskningsverksamhet, CRISPR-Cas9, genomredigering, geneditering, scenario		
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FOREWORD

Several representatives from the fields of research and business in plant breeding, animal breeding and medicine were interviewed for this report. In addition, a few representatives and board members of associations were interviewed. It should be noted that the research representatives were unanimous about the benefits of new genome editing techniques, and that on several occasions, these new techniques will even revolutionise development. These techniques enable us to significantly quicken and direct the creation of the correct variations.

The only general negative stance against the utilisation of new genome editing techniques was expressed by the companies operating on the consumer interface and by representatives of organic producers. Representatives of consumer production fear that the products will not sell, while the representatives of organic producers reject the utilisation of genome editing at least in plant breeding for strictly ideological reasons.

On a general level, our report also revealed that people do not know what genome editing is. At times, even the interviewed experts equated new genome editing techniques with gene manipulation. In addition, no one was able to explain the biological risk factors related to new genome editing techniques. The more evident, targeted risks are related to the misuse of techniques, such as terroristic purposes, or mixing the plants used in organic production with genome edited plants. Therefore, the rejection is not based on research information about the harms of genome editing techniques to people or to the environment.

However, it can be said that new genome editing techniques are dividing the society into those who support genome editing, based on the familiarity with the basics of the said techniques, and those who oppose them without knowing what they are all about. Therefore, the most substantial lesson of this report, in my opinion, is that gene aspects, including genome editing and new genome editing techniques, should be taught to people as per the views of the experts interviewed in this report, especially during upper secondary education. This would increase knowledge, and people would attain a better ability to decide whether they are for or against new genome editing techniques.

On behalf of the entire consortium, I would like to extend my deepest gratitude to all interviewees, the steering group of the project and to the researchers that were swept away by this fascinating topic.

Nina Wessberg, Leader of the Project Consortium
March 2021

GLOSSARY, LIMITATIONS AND APPLIED ABBREVIATIONS

Abiotic stress

Stress caused by environmental factors such as drought, heat, cold, light, and salinity.

ALLEA

The European Federation of Academies of Sciences and Humanities

BTNK

Advisory Board on Biotechnology under the Ministry of Social Affairs and Health

Convention on Biological Diversity, CBD

The secretariat of the UN Biodiversity Convention. Biodiversity refers to the richness of nature.

Cartagena Protocol on Biosafety

Biosafety protocol, a part of a larger UN Treaty that aims to ensure the environmentally safe use of gene technology.

Cisgenesis

Cisgenesis refers to a genome editing method, in which a new gene originates from the same or a cross-breedable species.

CRISPR-Cas9

CRISPR-Cas9 is a defence system against viruses, originally found in bacteria.

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) are DNA sequences that help bacteria to identify viruses that target them. These sequences function as memory in the defence system of the bacteria.

Cas9 refers to CRISPR-associated protein 9, an enzyme that cleaves DNA, i.e., a nuclease. With the help of CRISPR-Cas9, editing can be performed in a targeted way on the desired region of the genome, on the gene sequence. The Cas9 nuclease is guided towards the specific, targeted strand of DNA with the help of a corresponding RNA sequence (guide RNA). Then, the Cas9 cleaves the target DNA part. The method is also known as genetic scissors. The cell attempts to repair the DNA cleavage and attach the DNA strands back together (non-homologous end joining, NHEJ). Therefore, insertions, i.e., additional nucleotides or deletions, or omitted nucleotides, can occur. Nucleotides can also be altered to match a desired model (homology-directed repair, HDR). These alterations typically cause a mutation in the target area. CRISPR-Cas9 is one of the new genome editing techniques. In addition, the CRISPR-Cas9 technique enables the addition of a gene to the cleaved DNA sequence, in which case this research project will also entail the terms gene transfer, genetically modified organism (GMO), genetically modified, and transgenic.

DNA, DNA Sequence

Deoxyribonucleic acid is a polymer that encodes the organism's genetic material, the genome. DNA consists of deoxyribose sugar, phosphoric acid, and nucleotides A(adenine), C(cytosine), G(guanine), and T(thymine). Furthermore, DNA sequence refers to the sequence of nucleotides.

EPO Hormone

Erythropoietin

EPSO

European Plant Science Organisation

ETP

European Technology Platform

CJEU

The Court of Justice of the European Union

FAO

Food and Agriculture Organisation of the United Nations

FIMEA

Finnish Medicines Agency Fimea

Gene drive

A gene drive is a natural event that has been utilised in genetic engineering. With the help of a gene drive, the desired genes can be transmitted in a sexually reproducing population so that the probability of the offspring inheriting the said genes is higher than the frequency in normal population (50 percent probability according to Mendal's laws). Gene drives enable efficient genetic modifications of populations and even entire species with a very small number of modified individuals.

Gene editing, GE

The term gene editing is generally used as a synonym for new genome editing techniques, see new genome editing techniques.

Gene transfer technique, GM technique

Gene transfer techniques refer to all methods that transfer genetic material to the individual's genomes. Crossbreeding, in which an organism is developed towards the desired outcome through artificial means as orchestrated by humans and therefore quickening evolution, is not considered as a gene transfer technique.

Genetic engineering

Genetic engineering is a general term that refers to all methods that manage genetic material. These methods include GM techniques, gene transfer techniques, genome editing techniques, gene editing techniques, DNA techniques, RNA techniques, and cloning. The so-called classic mutagenesis techniques, such as irradiation and
chemical treatment, are not considered to be genetic engineering.

GTLK

The Board for Gene Technology under the Ministry of Social Affairs and Health

Gene therapy

Gene therapy treats diseases caused by defective or missing genes in somatic cells, that is, in all types of cells with the exception of gametes and their stem cells.

Genome editing

Genome editing is a range of gene techniques that edit the genomes of an organism by adding, removing, changing, or replacing parts of the DNA. Several different genome editing techniques have been developed (see new mutagenesis techniques below). The most recognised new genome editing technique is called CRISPR-Cas9. It should be noted that in this research project, the following terms shall be used: gene transfer, genetically modified, GMO, genetically modified organism, transgenic organism when referring to transferring a new functioning gene, regulatory sequence, or a combination of several parts of a gene (recombinant) as a part of the genome editing process.

Mutagenesis techniques

In this research project, mutagenesis techniques have been divided into new and classic techniques.

New mutagenesis techniques refer to genome editing techniques that enable for targeted, focused changes performed on the genomes. These techniques include, for example, CRISPR-Cas9 (see above), TALENs (transcription activator-like effector nuclease), and Zinc Finger Nuclease (ZFN). This research project applies the following choice of terminology: gene transfer, genetically modified, GMO, genetically modified organism, transgenic organism when referring to transferring a new functioning gene, regulatory sequence, or a combination of several parts of a gene (recombinant) as a part of the genome editing process.

The so-called classic mutagenesis techniques encompass methods such as irradiation and chemical treatment.

Genetically modified organism, GMO

Organism created with the help of gene transfer techniques; a synonym for transgenic organism.

Genetic modification technique, GM technique

A synonym for gene transfer technique

New Plant Breeding Techniques, NPBTs

See New Plant Breeding Techniques below.

Nucleotide

A building block of nucleic acid, i.e., DNA and RNA.

Recombinant

In this research, recombinant refers to a gene produced through a DNA-combination technique, which is transferred to the genomes of an organism. Furthermore, the gene can also be entirely synthetic, i.e., artificially constructed.

RNA, RNA sequence

Ribonucleic acid is a polymer that directs the synthesis of proteins according to its code. Ribonucleic acid consists of ribose sugar, phosphoric acid, and nucleotides A(adenine), C(cytosine), G(guanine) and U(uracil). RNA sequence refers to the sequence of nucleotides in the RNA.

Transgenic organism, GMO

A synonym for genetically modified organism.

Somatic cells, somatic

With the exception of gametes and their stem cells, all types of cells are defined as somatic cells.

Synthetic genomes

Synthetic genomes refer to chemically synthesised complete or nearly complete genomes.

TALEN

One of the new genome editing techniques, the transcription activator-like effector nucleases.

New genome editing techniques

The new genome editing techniques refer to methods, in which the genome is targeted and accurately edited. These new techniques include site-directed mutagenesis (through utilisation of directed nucleases to cleave targeted DNA (site-directed nucleases type 1 and 2 and oligonucleotide-directed mutagenesis)), cisgenesis, alteration of DNA methylation and synthetic genomes. In this research project, the following terminology have been applied: gene transfer, genetically modified, GMO, genetically modified organism, transgenic organism when referring to transferring a new functioning gene; regulatory sequence, or a combination of several parts of a gene (recombinant) as a part of the genome editing process.

New Plant Breeding Techniques, NPBTs

This term is generally used as a synonym for new genome editing techniques. However, the concept is notably more comprehensive; for example, grafting or graftage into a genetically modified rootstock or with a genetically modified scion. Furthermore, many other methods are placed in this category.

1 Introduction

New genome editing techniques enable for adding, removing, or editing the desired qualities of an organism accurately and in a focused way. For example, with CRISPR-Cas9 molecular or genetic "scissors", nucleotides in DNA can be added, removed or altered in specifically identified parts of the genome. To illustrate, plants' resistance to plant diseases have been improved with the help of molecular scissors, and currently, the technique is utilised in developing gluten-free wheat, among other things. By utilising genome information and new genome editing techniques, it is possible to develop even better treatment therapies for diseases caused by gene defects.

New genome editing techniques have been rapidly developed in the past few years, even to a point where new innovations and techniques are created every month. The name 'new genome editing techniques' is, therefore, a bit misleading since new techniques are constantly being created. Therefore, it might be more accurate to discuss targeted genome editing when referring to genetic scissors and gene editing, and differentiate between them and non-targeted genome editing, such as gene transfers or creating mutations through irradiation or chemical treatment.

Currently, genome editing is cheap and accurate. The number of biotechnological and similar companies as well as commercial applications that utilise genome editing has increased significantly. In fact, the market is considered to hold a great growth potential[1]. These new development paths and the new applications of existing technologies are raising remarkable questions from the perspective of the environment, society, and public health.

The new genome editing techniques can, for example, edit nearly any part of a genome with a properly designed guide RNA sequence, which is a significant improvement from prior techniques. In addition, effective genome editing techniques have a significant role in the framework of synthetic biology, as thousands of variants can be generated quickly, therefore considerably speeding Design-Build-Test-Learn cycles. The development of accurate genome editing techniques will also improve the development

1 Brinegar, K. (2017) *The commercialization of genome-editing technologies*. Critical Reviews in Biotechnology 37:7.

of gene therapies. The defective genes can be repaired accurately with the new methods, thus creating efficient treatment options for diseases and illnesses that have been either completely untreatable, inefficiently treated, only symptomatically treated, or treatable but not curable.

The Court of Justice of the European Union commented on the juridical position of the new genome editing techniques (also known as new mutagenesis techniques) in July 2018[2]. The CJEU ruled that organisms generated through new mutagenesis techniques belong to the category of genetically modified organisms (GMO). The GMO definitions are based on directives 90/220/EEC ja 90/219/EEC, decreed almost 30 years ago, and which, with the exception of the definitions, have been subsequently renewed (directives 2001/18/EC[3] and 2009/41/EC[4]).

Currently, only the so-called traditional mutagenesis techniques, such as irradiation and chemical treatment, which have a long history of safe use in plant breeding, are left outside the regulatory scope of the directive. This can create challenges, because for one, most organisms generated through the traditional and new mutagenesis techniques cannot be distinguished by any of the existing analysis methods. This specifically applies to the removal or addition of individual nucleotides. Moreover, if new mutagenesis techniques are used as gene transfer tools to transfer a gene to a genome, the techniques are regulated by directive 2001/18/EC. If the organism in question is a food or a feed, it is regulated in accordance with the regulation EC No 1829/2003. Furthermore, delivering GMO into the market is a long and expensive process.

The research and plant breeding communities especially are of the opinion that the 2001/18 GMO directive of the EU has become obsolete and is still based on the level of technologies from decades ago. The adherence to the GMO legislation makes bringing GM products to the market very challenging and expensive. Now, the ruling of the Court Justice of the European Union places the products that could utilise new genome editing techniques under this same regulation, making introduction of such products to the European markets nearly impossible.

During Finland's presidency of the Council of the European Union in 2019, the Council's decision to request the European Commission for a report on the current state of new

2 http://curia.europa.eu/juris/document/document.jsf?text=&docid=204387&pageIndex=0&doclang=EN&mode=lst&dir=&occ=first&part=1&cid=6972558

3 Directive 2001/18/EC of the European Parliament and of the Council on the Deliberate Release Into the Environment of Genetically Modified Organisms and Repealing Council Directive 90/220/EEC.

4 Directive 2009/41/EC of the European Parliament and of the Council on the Contained Use of Genetically Modified Micro-Organisms.

mutagenesis techniques and the regulatory development needs was accepted. The regulatory demand for new genome editing techniques in relation to the current EU regulation on gene engineering and international environmental agreements is, therefore, a very topical question.

In Finland, genetically modified organisms are regulated through the Gene Technology Act (377/1995), Medicines Act (395/1987) and Seed Act (600/2019), as well as by at least 15 other national laws and acts. Furthermore, the applicability of the new techniques is distributed under several different ministries. For example, the Ministry of Social Affairs and Health is preparing a new genome act, which proposes to secure the genetic data of an individual, containing data on possible mutations among other things. Genome editing of human gametes, however, is not ethically permitted in the EU, or anywhere else in the world. Therefore, this topic will not be discussed in this report. Regardless, when the intent is to develop treatments and therapeutic technologies that target somatic cells (i.e., cells excluding gametes) in genetic diseases, these aspects should also be considered.

The objective of the genome act under preparation at the Ministry of Social Affairs and Health is to create common ethical principles for handling human genome data. Furthermore, the act is meant to form a basis for a genome centre under the Finnish Institute for Health and Welfare (THL). The centre is meant to function as a keeper for the genome data collected from humans and as a centre of excellence. The centre does not, however, manage genome data and expertise related to other organisms, such as plants and animals. The Government's proposal for a genome centre on human health and genome data management is proposed to be presented to the Parliament in autumn 2021.[5] [6]

The differences between countries regarding the regulation of new mutagenesis techniques complicate the situation even further. For example, in the United States and Brazil, mutants generated through new mutagenesis techniques are not considered to belong under genetic engineering regulation, and this could significantly complicate international trade. From the Finnish perspective, there is a great call for more information on the state of new genome editing techniques not only from the perspective of the Finnish regulation, but also for the support of trade politics and regulation development. Information on the current and future needs and applications of the new technologies is required to form Finland's stance towards the regulation of new genome editing techniques.

5 https://www.eduskunta.fi/FI/naineduskuntatoimii/kirjasto/aineistot/kotimainen_oikeus/LATI/Sivut/genomilaki.aspx

6 VNK 2020. Innovaatiomyönteinen sääntely: Nykytila ja hyvät käytännöt. Valtioneuvoston selvitys- ja tutkimustoiminnan julkaisusarja 2020:27

Both the EU Commission and the UN Convention on Biological Diversity (CBD) are currently in the process of collecting background information on the utilisation and future applications of new genome editing techniques in the EU member states and CBD parties. In this report, the Finnish authorities and other stakeholders are offered background information on Finland's situation, specifically. Information on the current and future needs and applications of new genome editing techniques is required to form Finland's stance towards potential change proposals regarding regulations. This report secures the aforementioned demand for information.

1.1 Objective, Publishers, and Report Content

In this research project, the current content and extent of utilisation of genome editing techniques is clarified. The report includes research, product developmental and commercial utilisation. New business opportunities are identified through the needs of different fields and scenario analysis. It is significant to clarify, for various sectors, the different possibilities and demands for the utilisation of the techniques. In addition to the needs of basic research, agriculture, biotechnology, medicine, and environmental sectors, this report will acknowledge the potential import demand of organisms and derived products generated through new genome editing techniques from third countries, as well as Finland's export opportunities for the same.

In the research project here reported, an up-to-date understanding of the economic and public health significance of new genome editing techniques was formed. Furthermore, the health and environmental threats connected to genome editing are identified in the report, and the preparation demand of authorities connected to the said operations has been evaluated.

The **primary objective** of the project was to clarify the current and future needs and applications of genome editing techniques. Authorities will be able to utilise this information in their decisions on potential changes regarding regulations. Moreover, the report has established the societal and economic perspectives on genome editing techniques . Furthermore, the project clarified the business models enabled by genome editing techniques, as well as the realistic threats and opportunities connected to them. This report also assists in evaluating the impact of regulating genome editing techniques in different sectors, and therefore includes perspectives of economic impact, innovation, import, export, authorities' tasks and resources, the opinions of citizens, producers and other actors, and the impact on the SME sector and food production, medical use. Furthermore, when discussing agriculture, a specific question is raised by the organic sector's GMO ban. The research questions are presented based on the respective sub-projects in section 3.

The research project was carried out by VTT Technical Research Centre of Finland (VTT), Natural Resources Institute Finland (LUKE) and Demos Helsinki. VTT oversaw the execution of the project in its entirety, as well as the writing of this report. The principal investigator from VTT was Nina Wessberg. Santtu Lehtinen was responsible for the theoretical background, and they also participated in constructing the scenarios. Statistic material review was the responsibility of Mika Naumanen, while Anneli Ritala and Suvi T. Häkkinen provided their expertise on plant biotechnology.

Johanna Vilkki and Alan Schulman from LUKE offered their expertise in genomics and respectively in animal and plant breeding. In addition, Jaana Peippo from LUKE also participated in conducting the interviews for the project.

Demos Helsinki was responsible for the interaction with stakeholders in the project, as well as for the construction of the scenarios. From Demos Helsinki, Chris Rowley (transferred to other tasks from the project at the end of 2020), Satu Korhonen and Jussi Laine participated in the project.

In this report, the current state of genome editing, international scope and future are described from the perspectives of plant breeding, animal breeding and medical science. Business opportunities and realistic threats are included in the review.

1.2 Research Questions and Methods

The research project sought answers for questions related to three different aspects:

1. **CURRENT STATE: the current state of genome editing techniques in Finland by sector with a needs assessment**

   - To what extent are the new genome editing techniques currently utilised in Finland in basic research and in the agricultural, biotechnology, medical, and environment sectors?
   - For what purposes are the sectors currently implementing the new techniques? What kind of future needs can these sectors identify?
   - Do the aforementioned sectors have the ability and resources to utilise the said techniques on their own? If not, what kind of impediments are there?
   - How are the current use and potential future needs divided between the research and business sectors, as well as inside the said sectors? (basic research vs. applied research, SMEs vs large enterprises)

2. INTERNATIONAL SCOPE: Importing and exporting genome editing technique applications & international cooperation

- Is the potential use/need based on importing? If yes:
    - What kind of applications are in question? Are the applications organisms or products generated through new genome editing techniques?
    - Which countries are likely to export such applications?
    - What is/could be the potential volume of import?
- Do the different sectors have the need to import organisms generated with new genome editing techniques, products created through the said techniques, or innovations related to the techniques? If yes, to where would the importing activities be directed?
- What kind of international cooperation is involved with the techiques' use?

3. FUTURE, THREATS AND POSSIBILITIES: the impact and future development of utilising genome editing techniques

- To which direction do the sectors anticipate the new genome editing techniques to develop, during the next ten years in Finland and overseas? What is the economic significance of the techniques these sectors perceive?
- What kind of impact will the new genome editing techniques have on public health (impact of medication, vaccinations, gene therapy products or food)?
- What kinds of novel, realistic biothreats are connected to different applications of new genome editing techniques in each sector? To which of these threats the authorities should be specially prepared for in the opinion of the sectors?
- Is the use/non-use of these techniques connected to the national preparation for other types of threats (e.g., climate change, food security)?

The answers for the research questions were mainly reached through interviews, which were executed as theme interviews. This means that the topic discussion with the interviewee followed a prepared frame of questions (see appendix 1). The frame acknowledged and included all research questions. The interviews were recorded and transcribed for analysis. The interviews were carried out through remote connections due to the assembly and travel restrictions caused by COVID-19.

The total number of interviews conducted for this research was 49. One interview took about 30 to 60 minutes. The numbers of interviewees were distributed amoung

the sectors as follows: 17 research, 16 companies, six associations, six authorities or government, three funding and one from education.

The interviewees were chosen based on **actor analysis**, during which the key actors that utilise and develop new genome editing in Finland and overseas were identified. Actor analysis was complemented by the so-called snowball method, which means that each interviewee was requested to name potential additional participants. The interviewees were continued until repetition of the information gained from the interviews was identified. Therefore, reliably comprehensive data collection was achieved.

Actors connected to internationality and business were identified through a survey commissioned from Taloustutkimus Ltd. The survey measured the utilisation level of new genome editing techniques in businesses, the development of utilisation, needs connected to importing, as well as export potential. The survey was specifically oriented towards companies working with

- plants, cereals, crop plants,
- animals, cattle,
- meat and milk products and food processing
- gene therapies and treatments
- pharmaceuticals

Demos Helsinki delivered a register that contained the contact information of 132 actors to Taloustutkimus. Taloustutkimus updated the delivered register with the descriptive information of the company (such as revenue, personnel) and complemented the register with another contact information register printed from Bisnode Selector business data base based on the same actor information (a minimum revenue of two million euros was set as a delimiter). The data collection was carried out by phone interviews during November 5th until November 27th, 2020. The average time for one interview was about 12 minutes. Until the deadline, a total of 44 representatives of 43 companies were interviewed.

In addition, a literature review and two events that involved stakeholder groups were carried out in the project. These parts have been described in detail in the following subsections. The research material accumulated in the research project, including the interviews and workshop materials, were analysed, and worked into scenarios, which were then applied to outline the current and future needs and applications of new genome editing techniques (See Chapter 9, The Development of Genome Editing: The Scenarios).

Opening Meeting

To launch the project, a discussion event was organised on June 16th, 2020. During the event, the contribution to the research plan and key questions was collected from the stakeholders. Furthermore, a preliminary overall assessment on the current state of genome editing was formed, and the start of the project was communicated to all stakeholders. The detailed programme of the event is presented in appendix 2. The following organisations participated in the event:

From the ministries:

- Ministry of Social Affairs and Health
- Ministry of Economic Affairs and Employment
- Ministry of Agriculture and Forestry

From research organisations and universities:

- University of Helsinki
- University of Turku
- Natural Resources Institute Finland LUKE
- Folkhälsan Research Center
- Technical Research Centre of Finland VTT

From the private and third sectors:

- Association of ProAgria Centres
- The Finnish Medical Society Duodecim
- Association of Cancer Patients in Finland
- The Central Union of Agricultural Producers and Forest Owners (MTK)
- Nordic FoodTech VC
- Pharma Industry Finland
- Faba Cooperative Corporation
- VikingGenetics Finland
- Boreal Plant Breeding Ltd.

Stakeholder Event

In stakeholder meeting on December 12th, 2020, the results of the interview and survey studies were presented and feedback provided. In addition, the various future prospects of new genome editing techniques were processed. The event started with an introduction to the research project and with opening remarks on the current state of the new genome editing techniques based on the interviews and surveys. Thereafter,

the participants split into groups to discuss the need, regulation, attitudes, and business prospects of new genome editing techniques. The discussions were led by the facilitators of the research project.

The participants were divided into groups to clarify the new genome editing techniques' future potential and challenges from the perspectives of: 1) business, 2) daily life, and 3) society in 2030. The workshop procedures were based on co-creation methods. The stakeholder event programme has been included in appendix 3.

The following actors participated in the stakeholder workshop:

From the public sector:

- Business Finland
- Finnish Food Safety Authority
- Finnish Medicines Agency Fimea

From research organisations and universities, project funding:

- Natural Resources Institute Finland LUKE
- University of Helsinki
- Academy of Finland

From the private sector and company representatives:

- Finnish Bioindustries FIB
- Faba Cooperative Corporation
- Roal Ltd
- The Central Union of Agricultural Producers and Forest Owners (MTK)
- Finpom Ltd
- Lallemand Plant Care
- VikingGenetics
- Immuno Diagnostic Ltd

2 Theoretical Background

2.1 Societal Significance and Responsible Development of New Genome Editing Techniques

The new genome editing techniques have created revolutionary opportunities for a variety of applications in different fields: genome editing can be utilised, for example, in biological basic research, health care applications, plant breeding, and production of materials. One of the most significant applications could be in the field of health care. New genome editing techniques are applied to develop health care treatments and methods that can assist, for example, in better diagnosis, treatment, and even curing different hereditary diseases. For the food supply chain, new genome editing techniques are being applied to create tools to answer the challenges caused by climate change, food crisis, and population growth.[7]

The most popular genome editing technique is CRISPR-Cas9, developed in 2012. The application potential of the technique has expanded. To illustrate, in plant breeding, new genome editing techniques have enabled the generation of desired mutations in an accurate and efficient way, all the while reducing the time spent on the breeding process. Genome editing has quickly expanded to extensive use all around the world, and it is actively utilised in the development of various scientific and commercial applications in universities, research institutes, SMEs, start-ups, and large, multinational enterprises[8]. The market for products generated through new genome editing techniques is expected to grow from the current five billion dollars to over ten billion dollars by the year 2025[9]. Consequently, the demand for a competent workforce in the field is expected to grow significantly[10].

The new genome editing techniques have seen a rapid geographical expansion and versatile possibilities develop in the research and development activities of many fields. For example, the utilisation of CRISPR-Cas9 is relatively straightforward, which means that

7 Linturi 2020, 9–10.

8 Martin et al. 2020, 219–220.

9 See for example Sumant Ugalmugle & Rupali Swain. "Gene Editing Market worth over $10bn by 2026". Global Market Insights. October 1, 2020. <https://www.gminsights.com/pressrelease/gene-editing-market> [Accessed 17.2.2021]

10 Richard Gray, "Why gene editing could create so many jobs". BBC. 15th October 2018. <https://www.bbc.com/worklife/article/20181003-why-gene-therapy-will-create-so-many-jobs> [Accessed 17.2.2021]

it can be considered a ready, 'off-the-shelf' technique[11]. In addition, the fairly affordable genome editing techniques and their application possibilities make CRISPR-Cas9 and similar techniques available for even more actors[12]. According to some estimates, there could be even 100 000 laboratories and nearly one million researchers working with CRISPR-Cas9 all over the world[13]. However, the relative ease of use and extensive distribution of CRISPR-Cas9 also increase the potential misuse risk. In fact, CRISPR-Cas9 has highlighted new risks connected to biosafety, which have been noted by actors such as the US Intelligence Community[14].

Responsible application of genome editing techniques, such as CRISPR-Cas9, requires the support of extensive and professional societal discussion on the objectives, potential and limits. The ethical, juridical, and societal impact of new genome editing technique utilisation have been heavily debated among the experts. However, it is crucial that in addition to the experts, a larger audience and different stakeholders also participate in the conversation and present their own views, questions, and concerns[15].

The public interest towards new genome editing techniques is based on the various potential – direct or indirect, positive, or negative – impacts of their utilisation on the wellbeing of humans, animals, and natural habitats. It is crucial to manage this impact through public debate and democratic processes[16].

There is a special demand for a socio-cultural debate on the broad societal acceptance of genome editing techniques. Several previous examples of extensive scientific and technological innovations, such as nuclear power or GMO products, indicate that scientific evidence alone is not sufficient to provide understanding of the benefits and risks of these innovations; it also requires diversified dialogue. The disputes and conflicts centred around GMO products, specifically, are a great indication that a risk is both a political and cultural phenomenon that cannot be comprehensively managed from a purely technical perspective[17].

11 Nuffield Council on Bioethics Report 2016, 13,112–113.

12 Montenegro de Wit 2020.

13 Eric Niiler. "How Crispr could transform our food supply". National Geographic, August 10 2018. <https://www.nationalgeographic.com/environment/future-of-food/food-technology-gene-editing/> [Accessed 17.2.2021]

14 James R. Clapper. "Statement for the Record, Worldwide Threat Assessment of the US Intelligence Community". Senate Armed Services Committee. February 9, 2016. <https://www.dni.gov/files/documents/SASC_Unclassified_2016_ATA_SFR_FINAL.pdf> [Accessed 17.2.2021]

15 Bruce & Bruce 2019, 770–771.

16 Nuffield Council on Bioethics Report 2016, 21–22.

17 Jasanoff 2016, 89–90; Sarewitz 2015.

Furthermore, risk assessment should act as a base for a more extensive societal discussion on how and under which conditions the utilisation of new genome editing techniques would be acceptable. During the risk assessment, it would be beneficial to examine potential benefits and targeting in addition to potential disadvantages. Which potential benefits justify taking the risks? To which actors are the benefits and disadvantages focused on? Does the utilisation of new genome editing techniques benefit global justice, or do they cause inequality?[18]

On a general level, the public acceptance of the new genome editing techniques and other biotechnical and gene technological applications has not significantly changed during the past two decades. While most research communities adopt an enthusiastic attitude towards the potential of the new techniques, the greater audience is quite sceptical, especially towards genetically engineered foods, animals, and plants. However, the broad audience on the EU level has adopted quite a positive stance towards genetically engineered medical applications, such as new treatment methods[19].

New genome editing techniques have created revolutionary possibilities for science, health care, and the economy. However, currently, the public debate on genome editing is easily deteriorated to a two-sided debate on regulation, which places the safety and innovation values on opposite sides. One side proposes to create new possibilities to promote business and solve societal issues, while the other wants to ensure that the risks connected to the applications of new genome editing techniques are minimised as much as possible[20].

However, research conducted in Norway, for example, gives the impression that the discussion on new genome editing techniques is multifaceted, and not just a traditional black-and-white conflict. Although, in general, people portray that gene technology has its risks, many are still open and accept the utilisation of new genome editing techniques in battling climate change and reducing the use of pesticides, for example. Therefore, it is evident that the acceptance of genome editing is impacted by the objective of the technique, the benefits, and the beneficiaries[21].

Instead of the two-sided debate, there is a major need for a multi-voiced, data-based public debate, in which different genetic engineering methods and their impact could be differentiated from each other. Creating a debate such as this requires that the societal actors, the general audience, the scientists, and gene engineering applicators come together.

18 Biotekniikan neuvottelukunta 2018, 17–18.

19 Woźniak et al. 2021.

20 Habets et al. 2019, 22–23.

21 The Norwegian Biotechnology Advisory Board 2020.

2.2 Varied Applications of New Genome Editing Techniques

2.2.1 New Genome Editing Techniques as a Part of Agricultural Production and Plant Breeding

Farmers and plant breeders have been altering plant genomes for millenia. The objective of breeding has been to improve humankind's food security by developing crop production and resistance to plant diseases, for example. In addition, most crops utilised today have been generated by breeders judging and selecting individuals with desired traits from among variants carrying naturally occurring mutations, at a later stage mutations caused by chemical treatments or irradiation. These individuals are then utilised in plant breeding. The utilisation of the new genome editing techniques can be seen as a continuum from this tradition, and therefore, genome editing techniques are often called *new plant breeding techniques* (NPBTs). Depending on the perspective, new genome techniques can be also be seen as a more efficient and accurate extension of traditional breeding, or, alternatively, as a technical innovation that revolutionises the human–nature relationship[22].

One of the applications for the new genome editing techniques with the most potential is, in fact, plant breeding. Implementation of genome editing techniques offers new measures and tools for plant breeders to adapt crops to threats created by climate change, such as the increasingly variable weather and extreme climate events. Constant plant breeding is necessary to improve plants' resistance to various plant diseases and pests. Plant breeding is also crucial to answering the increasing global demand for food, while existing food systems are faced with more and more pressure[23].

However, the complex juridical position of genome editing techniques complicated their application to agriculture and plant breeding in the EU. First and foremost, the legal complexity is connected to interpretation of new genome editing techniques with regard to EU genetic engineering legislation. While the previous gene transfer techniques and GMO products are clearly governed by the genetic engineering regulations (2001/18), the legislative status of the new genome editing techniques has raised significant interpretative disagreement. The difference between the previous gene transfer technique and genome editing is the fact that in gene transfer, a gene with material from a single or multiple foreign species is transferred to a cell. As a rule, in genome editing techniques, a gene inside a cell is targeted, after which part or parts of its code is edited without adding any foreign material to the genome. Supporters of genome editing techniques argue that the technique's safety aspect resembles the traditional mutation breeding and previous

22 e.g. ALLEA 2020, 32–33.

23 e.g. Biotekniikan neuvottelukunta 2018, 16–17.

mutagenesis techniques, such as irradiation and chemical treatment, while still being considerably more accurate than these previous methods[24].

The decision by the Court of Justice of the European Union (CJEU) in summer 2018 commented on the legal position of new mutagenesis techniques, that is, on genome editing techniques. Based on the decision by the Court of Justice, organisms generated by new mutagenesis techniques, such as by genome editing, are governed by the genetic engineering directive 2001/18/EC[25].

2.2.2 New Genome Editing Techniques as a Part of Animal Breeding

According to the supporters of genetic engineering, breeding animals by use of genome editing would continue a long tradition of breeding, only in a more efficient and accurate way. However, when discussing animals, the application of the genome editing techniques encounters three challenges: the potential economic benefits, regulation of the technology, and the societal acceptance of the technology[26].

In theory, genome editing techniques could enable editing animal traits in a way that benefits both the animals and humans. Around the world, applying genome editing on livestock has been justified primarily with the well-being of the animals, because these techniques can, for example, improve the animals' resistance to different diseases and conditions. With the help of new genome editing techniques, swine resistance to infectious diseases has been improved; these diseases cause considerable suffering to animals and significant financial losses to producers. Genome editing techniques also offer the opportunity to lessen painful procedures performed on animals: polled cattle developed with these techniques help to minimise the risks and side-effects connected to horns and their removal for both the animals and care givers. [27]

Discussion on the use and acceptability of genome editing in animal breeding has so far stayed on the side lines, partially due to their difficult implementation in comparison to, for example, plant breeding. However, there is reason to ask about the ultimate objective of genome editing in animals. For example, is the animal's improved resistance going to be utilised to place even a greater number of animals in the same location? Questions

24 Eduskunnan tulevaisuusvaliokunnan julkaisu 2/2018, 9–13; Biotekniikan neuvottelukunta 2018, 19.

25 Court of Justice of the European Union. PRESS RELEASE No 111/18. Luxembourg, 25 July 2018. <https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf> [Accessed 18.3.2021]

26 Nuffield Council on Bioethics Report 2016, 58, 62–64.

27 Bruce 2017, 386–387.

regarding the application of genome editing are inevitably connected to broader questions regarding animal rights, well-being, and our industrial food systems.[28]

2.2.3 New Genome Editing Techniques as a Part of the Global Food System

Currently, the biggest challenges facing global food systems are climate change, population growth, and global competition for different resources. The two biggest drivers for food demand are population number and income level. The population of the world is forecast to grow to around 10 billion by the year 2050, while growth in income level increases the demand especially for milk and animal products globally.[29] To answer this increasing demand, the Food and Agriculture Organisation states that the global agricultural production should grow by 60–70 percent compared to the production level of 2007[30]. Genome editing is considered as one tool to solve these challenges related to increasing food production.

In this regard, it is beneficial to note that the models suggested to solve the global food problem are always dependent on the definition and presentation of tha problem. If genome editing is primarily utilised to further enhance agricultural production and the food industry, the global food problem tends to be defined primarily as a technological problem, and therefore, technological solutions are offered.[31]

However, several environment and non-government organisations are of the opinion that quantitatively, there is enough food produced in the world as it is, and therefore, the root of the food problem lies within the unfair global distribution of food. Thus, the technological solution of the problem easily bypasses the structural, political, and economic questions related to the food system functions. In addition, offering technological solutions often disregards questions on the ownership of the technology and who has the opportunity to utilise it. The sceptical non-government organisations have based their stance on the claim that the previous GM techniques applied on food production have been primarily utilised to promote the interests of food production systems driven by big enterprises. According to these non-government organisations, it

28 Anna Wilkinson. "Genome editing to improve farmed animal welfare. What's not to like?" 19 Feb 2020. Nuffield Council on Bioethics. <https://www.nuffieldbioethics.org/blog/genome-editing-to-improve-farmed-animal-welfare-whats-not-to-like> [Accessed 17.2.2021]

29 Tait-Burkard 2018, 1–2.

30 Alexandratos et al. 2012, 7.

31 Habets et al. 2019, 27; Bruce 2017, 394–395.

would be more beneficial to focus on reducing food waste and improving distribution than on enhancing food production.[32]

The supporters of genome editing techniques emphasise that while GMO cultivation focused on enhancing the intensive farming of large soy and corn fields, the new genome editing techniques are more focused on fulfilling the demands and wishes of the consumers and reducing the food waste. The benefits and simplicity of utilising genome editing techniques create opportunities for small and local businesses to participate in the market, while only the biggest, multinational enterprises can compete with GMO in the market. It is said that in addition to the better crops, the utilisation of genome editing techniques also gives a new method of developing products. This creates even healthier and more tempting products from the perspective of consumers. Therefore, utilisation of the new genome editing techniques is not only connected to enhancing the quantity or efficiency of food production; they can also be used to improve food quality, nutritional values, and other qualities.[33]

2.2.4 New Genome Editing Techniques as a Part of Ecology

Humankind's increasing ability to read and utilise genetic information changes the human-nature relationship. For instance, genetic information has been utilised in attempts to develop the resistance of humans, animals and plants to viruses and bacteria. New genome editing techniques can be utilised in, for example, generation of so-called gene drives. In the future, gene drives might be implemented in exterminating insects that spread various diseases, such as malaria, Zika virus disease, or dengue fever.[34]

Utilising genome editing in the production of gene drives to combat, for example, malaria, does encompass ecological and ethical dimensions on the level of ecosystems. Gene drive refers to a method that assists in spreading the gene edit quickly through the entire population. Therefore, gene drive enables downsizing or total extinction of different populations. The issue with utilising gene drives is the difficultly in carrying out risk evaluation with the current methods. Gene drive exposes living organisms to quick, extensive, and permanent ecological changes, whose impact is difficult to evaluate in advance. The possibility of being unable to revert the edited population back to its previous state has increased the risks of gene drives. To answer this issue, conditional gene

32 Montenegro de Wit 2020, 23–24; Nuffield Council on Bioethics Report 2016, 69–72.

33 Ashley Taylor. "Gene Editing Meets The Food Supply - The New World of Custom-Designed Crops". July 29, 2019. Milken Institute Review. <https://www.milkenreview.org/articles/gene-editing-meets-the-food-supply> [Accessed 17.2.2021]

34 Nuffield Council on Bioethics Report 2016, 76–77,80–81; Linturi 2020, 22–23.

drive systems are currently in development. These conditional systems would better limit the impact on a population level.[35]

2.2.5 New Genome Editing Techniques as a Part of Medical Science

In treatment methods based on genome editing, an entire gene is not transferred as in previous gene transfer techniques; instead, the DNA inside the gene is edited. The significant public health potential of new genome editing techniques is based on the assumption that on a theoretical level, a variety of different diseases could be treated with this new gene technique. [36]

Genome editing techniques and ever more affordable gene-based diagnostics have brought in new possibilities to improve people's health and wellbeing. The costs of sequencing a human genome have dropped from 100 million dollars to about a thousand dollars since 2001, which has enabled progressive more efficient utilisation of hereditary information for diagnostics or lifestyle recommendations, for example.[37] Gene-based diagnostics, combined with genome editing, create new possibilities for a better diagnosis of various diseases and individual treatments, which in turn can assist in more efficient treatments or even cures for several severe diseases in the future. [38]

When discussing medical genome editing in humans, it is essential to differentiate between genome editing on somatic cells and on gametes. Somatic editing impacts only the patient receiving the treatment and their cells, while editing the germline impacts gametes, which means that the changes will be inherited by the future generations, too. In health care, somatic editing has been applied to treatments of diseases such as HIV, haemophilia, and anaemia, while germline editing can be targeted to the development of naturally occurring resistance to infectious diseases.[39] However, it should be noted that editing the genomes of a human embryo is prohibited in the European Union on the basis of the Western science community's perspective and the EU Convention on Human Rights and Biomedicine.[40]

35 Biotekniikan neuvottelukunta 2018, 8,16; Wartiovaara 2017, 133–134.

36 Wartiovaara 2017, 130–133; Linturi 2020.

37 Halioua-Haubolda et al. 2017, 683–684.

38 Hirakawa 2020; Linturi 2020, 21–22.

39 Cavaliere 2019, 1–2; Max Planck Society 2017, 17.

40 The Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine. Convention on Human Rights and Biomedicine (ETS No 164) was opened for signature on 4 April 1997 in Oviedo (Spain). <https://www.coe.int/en/web/bioethics/oviedo-convention> [Accessed 18.3.2021]

2.3 Legal Position of New Genome Editing Techniques in the EU and on a Global Level

2.3.1 International Regulation of New Genome Editing Techniques in Plant Breeding

The international framework for regulating genome editing is multifaceted, entailing several laws and commitments. Currently, the Cartagena Protocol on Biosafety is the primary international agreement regarding the topic, despite the fact that some of the members have not signed or approved the Protocol. The purpose of the Biosafety Protocol is to promote global biosafety and minimise the risks to biological diversity and public health, based on precautionary principle.[41] In this section of the review, the focus is on the status of genome editing techniques in plant breeding.

Most of the national and international legislation on genetic engineering does not directly refer to genome editing techniques, because the technology in question is new, and it is utilised in numerous different fields. In agriculture and plant breeding, biotechnical applications are often considered under GMO regulations in one way or another.[42] The Cartagena Protocol uses the term Living Modified Organism (LMO), not GMO, and the question of whether gene-edited organisms are LMOs or not is controversial. In the EU and New Zealand, new plant varieties generated with genome editing techniques are governed by the existing GMO and biosafety legislation. Several members have applied and interpreted their existing GMO legislation in relation to the new genome editing techniques as well. The international and multifaceted regulation creates potential challenges to the global trade in food, plant varieties, and agricultural products generated through with the editing methods.[43]

The genetic engineering legislation of the EU is based on the precautionary principle, which proposes to prevent irreversible impacts on human health and the environment. The EU GMO directive 2001/18/EC regulates the marketing and deliberate propagation of genetically modified organisms in the environment. GM food and fodder, on the other hand, are governed by regulation (EC) 1829/2003. The products under the scope of GMO directives always require a risk assessment, which evaluates the direct and indirect impacts on the health of humans, animals, and the environment. The directive also includes the responsibility of monitoring, tracking, and recording the products.[44] The

41 Max Planck Society 2017, 17.

42 Menz et al. 2020, 2.

43 Schmidt et al 2020, 1–2; Ishii & Araki 2017, 7–9.

44 Habets et al. 2019, 10.

approval process of GMO products in the EU is demanding. The average costs of the five-year process for the applicant are around 10–15 million euros per product.[45]

In South America, the regulation and interpretation of the legal position of the new genome editing techniques has been taken the farthest on a global level. To illustrate, in 2015, Argentina was the first country in the world to revise their GMO regulation to include new regulatory criteria for new plant breeding techniques, such as genome editing. The criteria help to define the status of new organisms, varieties, and products on a case-by-case basis. According to the criteria, varieties that have been bred using genome editing do not belong under the scope of biosafety legislation and GMO regulation, if the variety does not include foreign genetic material. The regulation is based on a consultation process for a specific product, which helps to predict both the duration and costs of the process.[46]

Based on the preliminary results and experiences from Argentina, the country's new systems have assisted in the commercialisation of products (mainly food items) generated through genome editing. These products are developed by several SMEs, start-ups, and research institutes, which have become more numerous in plant breeding due to the new regulations. In addition, several businesses have specialised in generating specific traits and products.[47]

In the United States and Canada, it is completely possible to approve all foodstuffs generated through genome editing for market under the existing legislation.[48] Canada, in particular, is considered a model country for final product regulation, as the legislation does not differentiate between different plant breeding techniques. The product-based legislation of Canada is seen as flexible, and it does enable agricultural products generated by genome editing to be approved without updating the legislation. In fact, all agricultural products in Canada are regulated through the same legislative framework regardless of their production techniqe. Regulation is based on case-specific review of the new qualities of the new products.[49]

China is the global leader in utilising genome editing techniques, as measured by investments, launches, and patents. Surprisingly, despite the immense support of the government, China does not have an official legislative approach to genome editing. On the other hand, Russia has deemed GMO illegal in all other activities besides basic

45 Menz et al. 2020, 2.

46 Ishii & Araki 2017, 47–48; Menz et al. 2020, 7.

47 See e.g. Whelan et al. 2020.

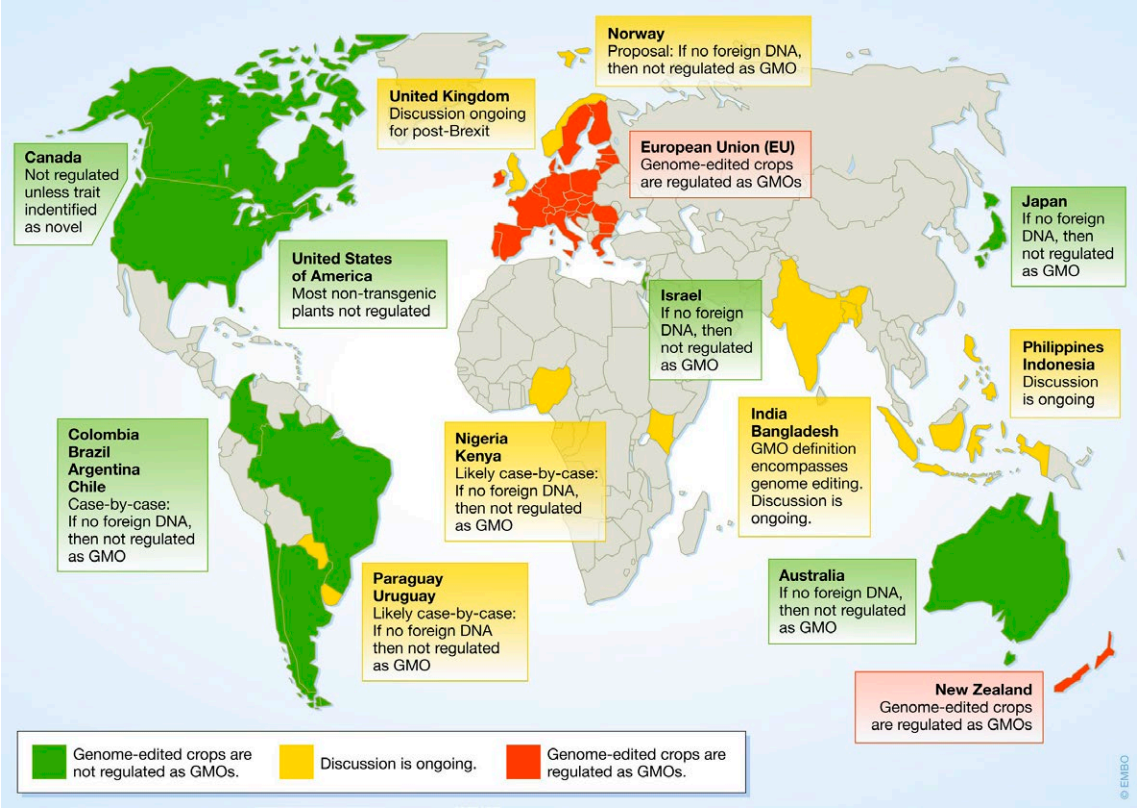
48 Menz et al. 2020, 4.

49 See e.g. Ellens et al. 2019.

research. However, the situation on applying new genome editing is undergoing change in Russia, because the government has directed significant investments to biotechnology, and especially to genome editing. In fact, Russia is expected to update its policy on genome editing methodology in the near future.[50]

Figure 1 portrays the various legislative interpretations of genome editing techniques around the world.

Figure 1. The legislative interpretation on new genome editing techniques in different countries. Source: Schmidt et al. 2020, 2.



2.3.2 Case Norway

On a global level, genome editing and new plant breeding techniques create a new challenge for current legislation, which is based on GMO products for the most part. One major question in the EU and all around the world is: 'should new genome editing

50 Menz et al. 2020, 12.

techniques be regulated under the GMO framework or by other means?' For this reason, the valuable trading partners of the EU, such as Switzerland, Norway, and Great Britain, are currently considering renewing the legislation on new genome editing techniques. One especially intriguing conversation on regulating and monitoring genome editing techniques is taking place in Norway.[51]

Among the Nordic countries, Norway clearly has the most non-conventional legislation on gene technology. The Norwegian legislation is based not only on comprehensive risk assessment and monitoring, but also on comprehensive evaluation of socioeconomic sustainability. The legislative assessment, therefore, is conducted in two stages: first, the genetic changes on the level of the organism used for the product are considered. Then, the broader societal impact of the product is evaluated and assessed. From the environmental perspective, the direct and the indirect, instantaneous, and accumulating impacts are examined in the evaluation.[52]

Furthermore, Norway has also expressed the desire to further develop their legislation through public debate. To promote the debate, the Norwegian Biotechnology Advisory Board presented their perspective on a new assessment and approval system in 2018[53], which would define the required level of assessment of genetically engineered products based on the level of genetic change (figure 2). The level of genetic change could be defined, for example, by determining if the same change could be achieved through traditional breeding methods, or if the change required DNA transfer between species.[54]

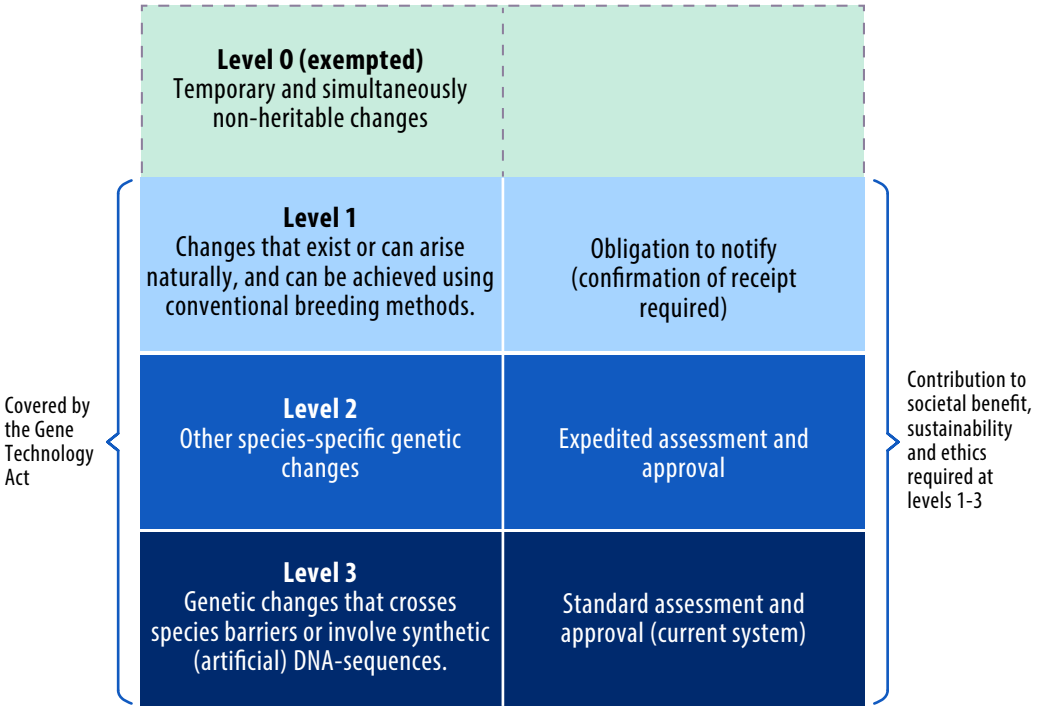
51 Schmidt et al. 2020, 2.

52 Myrh et al. 2020, 641–642.

53 The Norwegian Biotechnology Advisory Board 2018.

54 Eriksson 2019, 572.

Figure 2. The Norwegian Biotechnology Advisory Board's Suggestion for a Regulatory Framework on Gene Technology. Source: The Norwegian Biotechnology Advisory Board 2018.



2.3.3 The Stance of the Court of Justice of the European Union

In the EU, genetic modification and editing is mainly regulated with the Gene Technology Legislation of the Union. The most significant regulations on agricultural and food products are directives 2001/18/EC and 1829/2003/EC.[55] The field of genetic engineering, especially the utilisation of genome editing techniques in plant breeding and its legal position, has sparked interest during the past few years. The ruling of the Court of Justice of the European Union (CJEU) (case C-528/16) on new mutagenesis techniques on July 25, 2018[56] in particular raised a lot of discussion. As per the interpretation of the Commission, the ruling of CJEU indicates that the organisms created with the help of genome editing techniques belong under the scope of the GMO directive, and therefore, the corresponding responsibilities of registering, risk assessment, traceability, and monitoring are placed on products derived thereof.[57]

55 Max Planck Society 2017, 18.

56 Court of Justice of the European Union. PRESS RELEASE No 111/18. Luxembourg, 25 July 2018. <https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf> [Accessed 18.3.2021]

57 Ewen Callaway. "CRISPR plants now subject to tough GM laws in European Union". Nature 560, 16 (2018) <https://www.nature.com/articles/d41586-018-05814-6> [Accessed 17.2.2021]

According to the CJEU ruling and the interpretation of the Commission, utilising new (post-2001) mutagenesis techniques, as well as genome editing on plants or other living organisms is considered regulatable genetic modification. Therefore, the definition in the GMO directive applies to all organisms that have had their genetic material altered with a mutagenesis technique. Only the 'traditional' mutagenesis techniques developed before the GMO Directive came into effect (in 2001) are not considered to belong under the scope of the Gene Technology Regulations of the EU. Chemical and irradiation mutagenesis are examples of such techniques. As a consequence of the ruling, the organisms generated through the new genome editing techniques and genetically modified organisms are not differentiated in legislation: both belong under the scope of GMO legislation, and both include the same responsibilities.[58]

This association has stirred a lot of controversy especially among scientists, who have highlighted the differences between new genome editing techniques and gene transfer methods. Per the perspective of the majority of scientists, genome editing techniques are more comparable to traditional mutagenesis than to gene transfer techniques.[59] According to this perspective, there is no scientific reason or evidence for regulating traditional and new mutagenesis in different ways, because the utilisation of new genome editing techniques produce the same results as the traditional breeding methods, only more quickly and accurately.[60] For example, with irradiation random changes are produced in the DNA, and then the plants with the desired traits are chosen from among all others. Whereas genome editing enables generation of specific changes in parts of DNA known to give the desired traits. In fact, the ruling of CJEU has been described thusly: while the 'dynamite fishing' of traditional methods is legal, 'angling' through new genome editing techniques is prohibited.[61]

However, several environmental and non-governmental organisations have emphasised that there is still not enough information on the long-term impact of genetic engineering on the environment, people, and animals to reliably evaluate their safety. These actors highlighting the precautionary principle are of the opinion that organisms generated through new genome editing techniques belong strictly under the regulative framework of the GMO directive.[62] The suspicions placed on new genome editing techniques are heavily influenced by fears of genetic engineering in general and the view that traditional food production is organic. In general, people are against genome editing techniques for the same reasons GM methods are strongly opposed: both are seen to encompass

58 Wasmer 2019, 4–5.

59 ALLEA 2020, 8.

60 ALLEA 2020, 8.

61 Schulman et al. 2020, 8.

62 Habets et al. 2019, 12–13.

potential, significant risks to the ecosystem. Furthermore, people are afraid of accidental, so-called off-target mutations.[63]

Currently, the precautionary principle and securing the traditional European agriculture and food industry are strongly emphasised in the EU regulation. Innovations of new genome editing techniques and other biotechnical methods are seen as a threat towards traditional food production. The current regulation causes products with the same qualities to fall under the scope of different regulations based on the applied techniques. This, in turn, places the products in unequal statuses.[64]

2.3.4 Potential Consequences of the CJEU Ruling

The ruling of CJEU was a massive disappointment to European plant breeders. To illustrate, the European Federation of Academies of Sciences and Humanities ALLEA has encouraged the EU to reconsider the legislation on new genome editing techniques. According to the critique, the legal position of new genome editing techniques requires additional practical clarification and guidance. During Finland's presidency, the Council of the European Union did, in fact, request the commission to perform a review on the legal position of new genome editing techniques and its implications, which has been completed for delivery at the end of April 2021.[65]

As of now, the ruling of CJEU is feared to be the death blow to research and development activities on new genome editing techniques, and to the commercialisation of the products created through these techniques in Europe. As a consequence of the ruling, the investments in the field are likely to diminish, since the long and expensive approval process that follows the current legislation makes the commercialisation of the varieties generated through new genome editing techniques extremely difficult. The only actors capable of executing the commercial utilisation of genome editing in the EU are large, multinational enterprises.[66] Even large companies that focus on agricultural products,

63 Eric Niiler. "How CRISPR could transform our food supply". National Geographic, August 10 2018. <https://www.nationalgeographic.com/environment/future-of-food/food-technology-gene-editing/> [Accessed 17.2.2021]

64 Eduskunnan tulevaisuusvaliokunnan julkaisu 2/2018, 11–12.

65 Van der Meer et al. 2021, 3,9–12. The report was published right before the publishing date of this report in the end of January 2021: COMMISSION STAFF WORKING DOCUMENT Study on the status of new genomic techniques under Union law and in light of the Court of Justice ruling in Case C-528/16 https://ec.europa.eu/food/plant/gmo/modern_biotech/new-genomic-techniques_en.

66 Schulman et al. 2020, 9–10.

such as Bayer and BASF, have threatened to move their genome-editing plant breeding functions outside Europe due to the CJEU ruling.[67]

In Europe, lagging behind the frontline of global research and development work has caused concern. EU Member states are world-leading actors in research that uses genome editing. However, even now, they are significantly behind China and the United States on commercial application of the research.[68] Currently, only eight percent of CRISPR patents are allocated in Europe, while nearly 60 percent of them originate from China, and 26 percent of the patents have been applied from the United States[69].

In addition, the EU treats agricultural products generated through new genome editing techniques differently from their trade partners all around the world. As of now, marketing of the varieties generated through new genome editing techniques requires extremely extensive risk assessment processes that follow the GMO directive. Based on the producers' experiences, importing GMO species to the EU costs about 10–15 million euros on average, and it takes several years[70]. In other words, EU regulations create a significant barrier for marketing varieties generated through new genome editing techniques, since these species are considered GMOs.[71]

In addition, many fear that implementing the principles of the CJEU ruling will also lead to disruptions in the international trade of agricultural products. To illustrate, the legislation in Argentina, Brazil, and the United States, which import over 30 million tonnes of soy to the EU, does not require their producers to register or track varieties or foodstuffs derived thereof, which are generated through new genome editing techniques, as is the case in the EU. Despite this, the varieties under the scope of the GMO legislation of the EU, such as the above-mentioned genome edited soy, must be approved, and registered before these varieties or products therof can be released to the internal market. However, the issue with varieties generated through new genome editing techniques is that the authorities do not have the necessary technological means to identify them. Indeed, the scientific view is that many changes made by genome editing are impossible to distinguish from ones occurring naturally or by traditional mutagenesis. This means that it is nearly impossible to trace and control the plant breeds generated through genome editing techniques in accordance with the demands from the current GMO legislation of the EU. Therefore, trade with certain countries will either be halted, or varieties generated

67 Reuters. "Bayer, BASF to pursue plant gene editing elsewhere after EU ruling". July 27, 2018. <https://www.reuters.com/article/us-eu-court-gmo-companies-idUSKBN1KH1NF> [Accessed 17.2.2021]

68 Menz et al. 2020, 14.

69 Schmidt et al. 2020, 1.

70 Schulman et al. 2020, 9.

71 ALLEA 2020, 26–27.

through new genome editing techniques are definitely going to end up in the EU region as a part of international trade.[72]

In addition to the economic and legislative challenges, one of the most frequently expressed concerns is the delay on the development of sustainable agriculture and means to combat climate change through plant breeding caused by the current EU ruling on the utilisation of the new genome editing techniques. Fulfilling the objectives of sustainable development by the year 2050 with available water, less fertilisers and smaller acreage requires new and improved varieties. New varieties generated through genome editing are perceived as a crucial method to answer the increasing demands of food production, as well as the global challenges of climate change and population growth.[73]

There appears to be three potential future options: continuing the current regulatory framework, adapting the current framework, or creating completely new legislation on the topic. At the end of this report, the future of the new genome editing techniques in the EU is discussed in detail in scenarios devised within the framework of this study.

72 Eriksson et al. 2019, 1678–1681; ALLEA 2020, 30.

73 Schulman et al. 2020, 10.

3 Actors Utilising New Genome Editing Techniques in Finland

To gain an overall view, the attempt was made to reach a field of actors who could have insights into the development in the field and its requirements. The actors we came across within this study can be divided into three groups: 1) scientific communities and research institutes; 2) government, organisations, and foundations; 3) companies.

3.1 Scientific Communities and Research Institutes

The utilisation of new genome editing techniques both in Finland and in Europe relies heavily on science and research. Therefore, there are many institutes conducting research or developing new applications based on genome editing techniques in Finland as well. During this study, at least the following 15 domestic and international organisations were identified. They are already operating and in central positions in the research and development of genome editing techniques:

- Biomedicum Stem Cell Center (BSCC)
- Cost Action: Genome Editing in Plants - a Technology with Transformative Potential (PlantEd) CA18111, University of Lund, Sweden)
- European Plant Science Organisation (EPSO)
- European Technology Platform – Plants for the Future
- University of Helsinki
- University of Eastern Finland
- KCT Kuopio Center for Gene and Cell Therapy
- National Resources Institute Finland (LUKE)
- Institute for Molecular Medicine Finland (FIMM)
- Finnish Environmental Institute (Syke)
- VTT Technical Research Centre of Finland Ltd (VTT)
- Finnish Institute for Health and Welfare (THL)
- University of Turku
- Åbo Akademi University

3.2 Government, Organisations and Foundations

In the context of new genome editing techniques in this study, we have established the following actors to hold key positions in the public sector. Furthermore, they are also connected to the central fields of application in new genome editing techniques:

- Advisory Board on Technology (BTNK)
- Board for Gene Technology (GTLK)
- National Cyber Security Centre
- Ministry of Agriculture and Forestry of Finland
- Ministry of Justice
- Ministry of Education and Culture
- Finnish Food Authority
- Ministry of Social Affairs and Health
- Finnish Institute for Health and Welfare (THL)
- Finnish Transport and Communications Agency (Traficom)
- Finnish Safety and Chemicals Agency (Tukes)
- Ministry of Economic Affairs and Employment of Finland
- Ministry of the Environment

The project also identified organisations and foundations, which the researchers could link to questions related to the new genome editing techniques. However, the organisations and foundations did not acknowledge their connection to genome editing techniques and therefore did not feel that they were suitable to be interviewed for this study. The organisations and foundations that potentially have viewpoints on utilisation of genome editing were identified in the study to be the following:

- The Finnish Institute of Bioethics
- Euroseeds (a European organisation dealing in seed trade)
- The Finnish Network for Rare Diseases (Harvinaiset-verkosto)
- Pharma Industry Finland
- MyData Global
- Open Knowledge Finland
- The Finnish Medical Society Duodecim
- Suomen potilasliitto ry (an association for Finnish patients)
- Finnish Federation for Social Affairs and Health SOSTE
- Association of Cancer Patients in Finland
- Cancer Foundation Finland

3.3 Companies

One purpose of the study was to generate new information on the companies' different utilisation needs and manners in the context of the new genome editing techniques and to survey the needs and potential especially for business. Companies were represented in the interview part of the study, in a survey study carried out by the Market Research Company designed for firms, and as a part of a joint development event for a variety of actors.

Companies and foundations from various fields took part in the interview, stakeholder, and survey study. In total, 68 business representatives were reached: 16 were interviewed, 8 participated in stakeholder events, and 44 answered to a survey. Furthermore, some of the actors took part in several stages of data collection for the study. The fields of medical research and development and biotechnology research, as well as the industry of chemical manufacturing, were strongly represented.

The lines of business of the companies that participated in the study:

- law firms
- biotechnology research and development
- food industry products
- food products
- chemical products
- lab equipment and supplies
- fertilisers and pesticides
- medical research and development
- farming
- agricultural services
- agriculture
- dairy farming
- measuring and research equipment
- financing
- industrial chemicals
- health care
- health service consultation
- wholesale
- product development, research, and design services
- vegetables, fruits, and berries

In addition, the following business branch organisations were reached:

- Pharma Industry Finland
- The Central Union of Agricultural Producers and Forest Owners (MTK)
- Association of ProAgria Centres
- The Finnish Medical Society Duodecim
- Finnish Bioindustries FIB
- Association of Cancer Patients in Finland

The Market Research Company interviewed 44 business representatives from 43 different companies in a separate survey. Nearly half of the interviewees were located in Uusimaa province. The most common of job descriptions of those interviewed were manager, director of research, or CEO. The most common lines of business were medical research, biotechnology research, and diverse manufacturing of chemical products. Additionally, the team of researchers interviewed a total of 49 actors relevant to genome editing techniques from the public and private sectors, 16 of whom were company representatives.

4 Plant Breeding and New Genome Editing Techniques

4.1 Current State

In the **plant breeding** context, genome editing is applied in **basic research** to a growing extent. In basic research, field experiments are carried out on, for example, genome-edited trees. Genome editing is an alternative to producing mutations otherwise achieved by irradiation or chemical means or by finding natural variants. With the help of new genome editing techniques, mutations can be precisely targeted to the desired parts of the genome, thus reaching the wanted results faster. Compared to the new genome editing techniques, irradiation and chemical mutagenesis are hugely random; one of the clear advantages of the new genome editing techniques is the fact that the desired effect does not have to be searched for among literally millions of random mutations, as you have to do with irradiation and chemical mutagenesis. To use the new genome editing techniques, you need precise information on the plant genome, so that the mutation can be localised to the desired place. Therefore, the practice becomes sensible and more efficient for the plant breeding process.

In basic research, new genome editing techniques are used to discover the various genetic basis of many different phenomena occurring in plants, such as development and growth, biosynthetic pathways, or disease resistance, in order to produce the desired traits. It must be noted that in plant breeding, the breeding of a good, quantitative gene basis is still done with methods other than genome editing, for example, by crossbreeding and selection. This is because thousands of genes contribute incrementally to elite performance, whereas genome editing aims to edit only one or a few major genes at a time. It became apparent in the interviews, that when it comes to basic research, no great obstacles were seen in the utilising of new genome editing techniques.

> ***'It speeds up plant breeding. In principle, the technique is an alternative to mutagenesis, where you try to induce mutations by irradiation or by chemical means, and then you try to pick those that are suitable'*** [research representative]
>
> ***'It is a Finnish job, they found out how a tree grows in girth, what genes contribute towards it. If you can mess with the genes of trees, and they grow a per cent more in girth and the budget of UPM Kymmene is like 10 billion. I mean, go ahead and count what one per cent on top of that means.'*** [researcher of medicine]

At the moment, a lot of the research on plant biology and breeding is done by using the CRISPR-Cas9 genome editing technique. This and improved methods (such as new enzymes to replace Cas9) are constantly being developed to make the editing process better and more efficient. It was discovered in the interviews that research and development of genome editing methods were deemed important and that the work done on this needs funding.

> ***'I wish the sponsors would get the message, that they shouldn't be shy about investing in this research related to gene editing ...that even with the big question mark as to what the utilising part is exactly, we still should be able to develop the techniques. They aren't ready yet to be used in plant breeding'*** [research representative]

In practice, the new genome editing techniques are not being applied in Finnish plant breeding. There are two main reasons for this: 1) in European legislation, the results gained with the help of genome editing are currently handled as a part of the GMO legislation, and this raises the costs of the required risk assessment to an intolerable level, and 2) in general, consumers at the moment have a negative view of GMO products, to which products produced with the help of genome editing techniques are now being contrasted. In food industry, commodities produced with the help of genetic engineering exist only in the form of enzymes. In addition, proprietary rights and patents related to new genome editing techniques are quite unclear and make the use difficult, which, in turn, is reflected on the applications and commercial use.

> ***'Everybody is probably interested in this. And there's a big difference here in the sense that they won't really get into applications in Europe, because it resembles genetic modification. The same kind of restriction as in genetic modification, that there are about two traits on the market, there are other smaller ones, but two main traits and this is not because we don't have ideas, but it's because it's been made so expensive that in practice only these giants can do it, and even they do it only with a few plants. ... Rather the problem is that this has no appeal for applications and that's why the funding rejects it.'*** [research representative]
>
> ***'I'd say that as long as the consumers don't openly embrace genetically modified food, then the food producers won't want it either and that's how long we can't take it either. It all starts with the consumers' trust.'*** [business representative]
>
> ***'what's in bad shape, in my opinion, is this information on genetic modification techniques directed at the public. Quite a few people may still have the slightly misinformed idea, that genetic modification techniques would create some monster plants or destroy all wild plants in Finnish nature. It's highly unlikely for***

> ***this to happen. Most often our genetically modified plants are such, that they probably couldn't make it out there in nature. In my opinion, they could pay more attention to things like these when educating the public.'*** [research representative]

4.2 International Scope

All in all, the seed trade is an extremely international business. There are no plant varieties produced with the help of genome editing on the European market, but they are available elsewhere in the world. Countries to most likely engage in the export and import of genetically modified plants would be those countries that have utilised GMOs, which probably means at least Canada, the U.S.A, Brazil, and Argentina. As for China, things are unclear, even though China is considered in many ways to be a pioneer in developing genome editing techniques. It seems, that for example, in the US and Asia, the legislation is more advanced than its counterpart in Europe, and consumers more mature in terms of their acceptance, which translates to better export opportunities. It was observed in the interviews that exporting genome editing techniques within Europe would work well for smaller plant breeding companies, whereas large companies would produce the needed varieties themselves. It was considered important for Finland to maintain plant breeding, and therefore be able to provide good, competitive varieties for Finnish farmers and for the export to Scandinavia and the Baltic countries in particular. When talking about importing and exporting, border control was seen as a problem, because no detection methods suitable for genome edited plants exist. Thus, monitoring is impossible.

> ***'if we do good plant breeding here in Finland, then yeah, the seed will surely have export potential in Scandinavia and Baltic countries. ---- our... grain market pretty much thrives on this, and exporting of oats is the most important one for us. And if we don't have domestic breeding, and when you apply this technique and keep breeding better and better varieties all the time, then you can truly do some exporting.'*** [farmer]
>
> ***'If we don't see a market in European Union, I am guessing that they will go for other markets because of regulations. (If) they cannot get market authorization or authorization for commercialization in the European Union, they will not get any further.'*** [organisation representative]

There is a lot of international co-operation in genome editing research, and Finnish research teams are well linked within Europe and globally as well. At the moment, international cooperation takes place, among other things, in the form of sharing genome editing-related components globally, and as actual joint research (international research consortiums, conferences, publishing, education). Exchange of information, workshops,

symposiums and the like are organised by various organisations, such as EPSO, ETP, Euroseeds, and they also take place within Nordic networks and NATO. In the EU, there are always ongoing activities related to the preparing of various guidelines and the unification of legislation. On an international scale, the Convention on Biological Diversity and the Cartagena Protocol on Biosafety form a framework for cooperation. In the context of safety aspects, Science and Technology networks and Nordic-Baltic cooperation were mentioned.

> ***'introduction would probably be like, you know, in co-operation with one of those labs, where this technique is employed on the species of interest, so that whether it's a prototype plant, Arabidopsis or some cultivated plant, we'd go to the lab to learn the technique and transfer it to our home lab.'*** [research representative]
>
> ***"harmonisation of regulatory landscape on a global level is very important to be able to specially for those technology to be able to apply them and also to move seeds around the world."*** [organisation representative]

Figures 3–5 portray the dispersion of plant research related scientific publications in terms of techniques, researching countries and researched species. In genome editing, use of CRISPR techniques rose sharply since 2015. China and the USA are in the lead in utilising genome editing, and rice is the most popular researched plant. In Europe, barley is clearly an important target for genome editing.

Figure 3. Publications related to genome editing during the past years in the world (* 01-05/2018). Source: Modrzejewski et al. 2019.

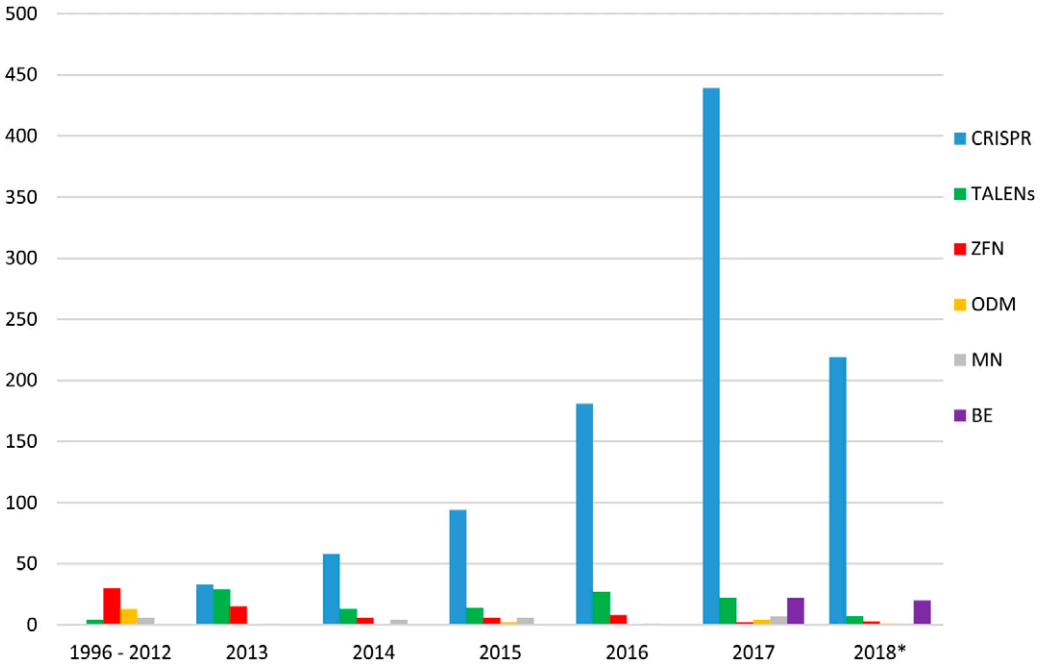


Figure 4. Published research reporting on genome editing by country up to 5/2018. Source: modified from Modrzejewski et al. 2019.

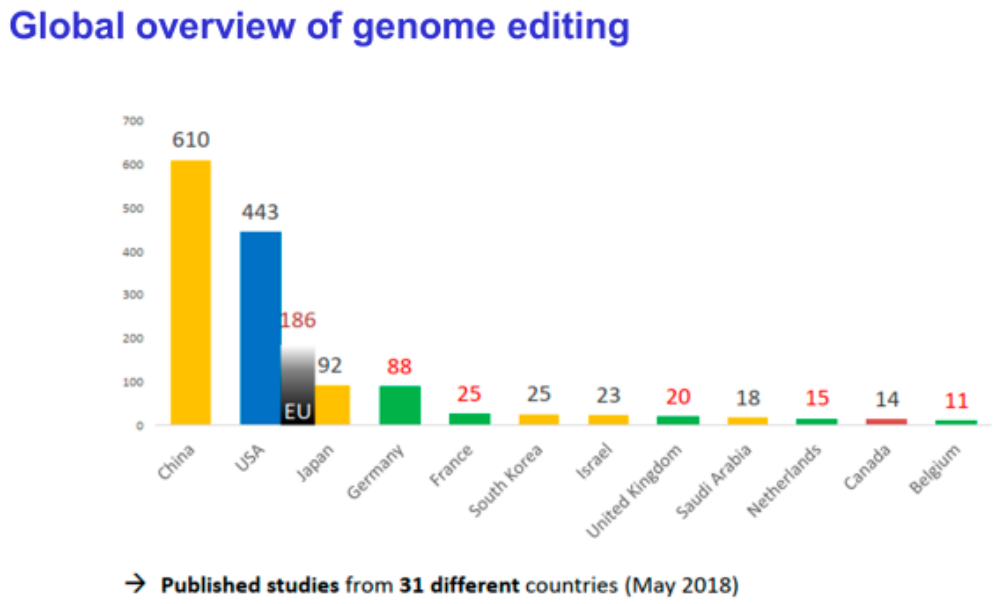
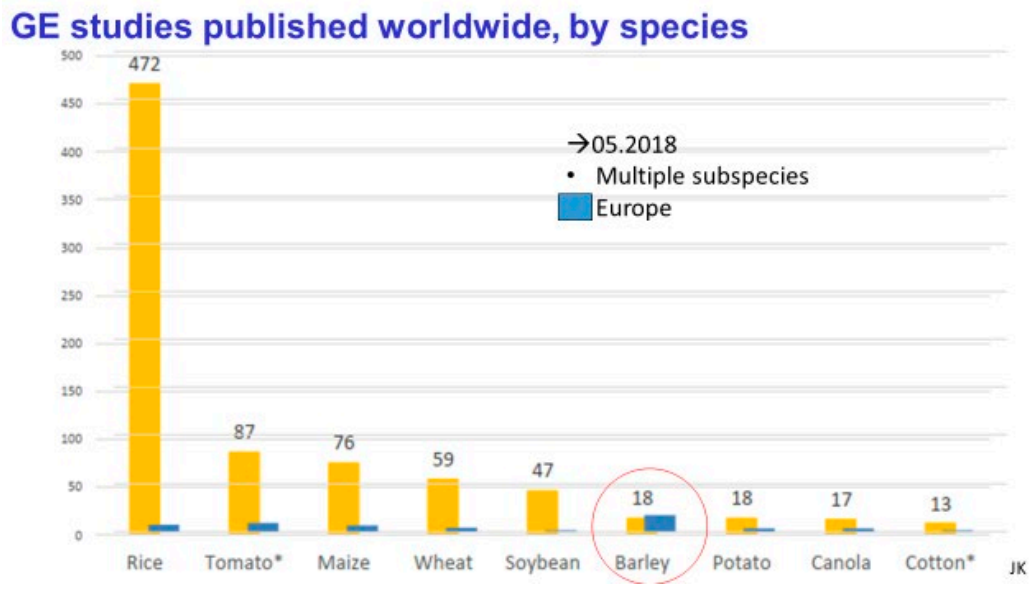


Figure 5. The use of genome editing in research publications by species up to 5/2018. Source: modified from Modrzejewski et al. 2019.



4.3 Future: Threats and Possibilities

In terms of plant breeding, the introduction of genome editing techniques in the future was considered quite uncertain in Europe. On a global scale, roughly 17–30% of companies plan to introduce a product developed with the help of genome editing on the market within the next five years, while 36–67% of the companies estimate the scope to be 5–10 years and 0–50% of companies 10 years. On the other hand, 33–45% of companies state that they have delayed their marketing plans due to the current regulatory situation. If products manufactured with the help of new genome editing techniques were not under the same regulation as the GMOs, up to 80–85% of companies would utilise genome editing. People especially hoped for the assessment of both the risks and benefits to be estimated side by side within the genome editing techniques' risk assessment.[74]

The poor position of the EU as an innovator and a contributor of these technologies was strongly brought up in the interviews. There is a clear conflict between the fact, that on one hand, basic research on new genome editing techniques is being funded in the

74 Jorasch P (2020) Potential, Challenges, and Threats for the Application of New Breeding Techniques by the Private Plant Breeding Sector in the EU. Front. Plant Sci. 11:582011. doi: 10.3389/fpls.2020.582011

EU, yet on the other hand, the prospects of applying them are quite limited. **One of the greatest threats was thought to be that plants produced by new genome editing techniques were juxtaposed with GMO plants in Europe.** There is a strong call for a change because it is apparent that Europe is already lagging behind the global progress, as far as these techniques are concerned.

> ***'In the time frame of 10 years, I'd be so happy to see the legislation in Europe to change, but when you look at the current state, I doubt that even after 10 years we won't be in a place, where products manufactured by the CRISPR-Cas9 technique are not genetically modified. I hope this wouldn't be the case, but in my opinion, the progress isn't always going to a good direction.'*** [research representative]
>
> ***'the EU is the big question mark here, the judgements done in the EU are in the focus, so we could know, if we even get – with what kind of a schedule we will get, can we change the interpretation of the law at least to an extent that allows some of the simplest editing techniques to be employed within a 10 year perspective, but it may be, that if we start changing the entire GMO legislation, 10 years may be a short time span for that – I hope we could get some sort of permit for doing something on editing somewhat quicker from the EU; if they start to consider these as mutations, simpler genome editing techniques to be mutation technology, so that a certain species doesn't have to be labelled in some special way.'*** [company representative]
>
> ***'But it's just the case then, that it's no longer in the hands of us Europeans anymore, this plant breeding. Then we are in a serious situation. ---if it was to be, that we couldn't use the technique, you won't see it in five years. But it's going to show in ten, 20 years, and when we do notice, then what will we do? It will be late by then.'*** [farmer]

Apparent, realistic threats did not surface in the interviews. For example, the potential formation of allergens or toxins was usually mentioned, but it was stated that this would be noticed in the normal process of new products coming on the market. This is something all products go through, regardless of how they are developed. **Home use enabled by technologies, potential intentional misuse, biohacking, and the manufacturing of chemicals or biochemicals** were also mentioned in the interviews. On the other hand, **potential unintentional misuse** came up. From the perspective of organic production, the greatest threat is that **organisms produced with the help of new genome editing techniques contaminate organic products**, but then again, the same threat exists for the traditional non-organic products.

> ***"There always the possibility, it's the same with conventional breeding. You could always end up with a product that will be hazardous, because the combination of these and these traits actually could, for example, create an allergen, new allergen or some kind of toxin. That is always a possibility, but again, this is something that is tested for, for any new type of product that goes on the market, so regardless of the tool used."*** [organisation representative]
>
> ***'In my opinion, it's sensible to think about and screen for threats in a sensible scale all the time, and for instance these guide RNAs they put that would remain transgenic, that is, the plant would remain transgenic to prevent viral infection, for instance, so it would target the virus genome, then the virus genome surely can also mutate there and maybe escape from the system, but at the same time, like, are there any chances for off-targets to then form up, you got to keep an eye out for this. Then, what the authorities should especially be prepared for, what we'd want, in my opinion they should have a good idea of the possibilities and the threats and think about the balance between those two. And be conscious of what can be analysed, tracked, and what can't be.'*** [research representative]
>
> ***'If you compare varieties produced by irradiation breeding, those produced by traditional cross breeding, transgenic organisms or gene edited varieties, I don't personally see any significant threat to biosafety.'*** [plant research representative]

Biothreats may emerge especially with the use of gene drives. To illustrate, **decreasing the number of insects spreading pathogens by using the gene drive method could cause ecological effects on plants through entomophily**. In general, the emerging threats are influenced by the organism's traits achieved by mutation, regardless of the technique those mutations were generated by. Thus, the threats previously recognised with the use of genetic engineering, which would be connected to, for example, the survival and spreading of a gene edited/genetically engineered organism in nature and the spread of the mutated trait in populations in nature, do not necessarily disappear by switching techniques.

The effects of climate change on the spread of insects and pollinators were also seen as a pressure we should be prepared for. New plant diseases or a change in pollinator diversity were considered to be great economic factors, as they would result in crop loss, among other things. **With plants produced by new genome editing techniques, we could deal with these indirect climate issues more efficiently.** Similarly, cultivated plants applicable and bred for a specific environment and geographic location at this point do not necessarily survive in rapidly changing climate conditions. Therefore, it is important, for example, for the northern countries to have self-sustained technology for future needs.

> ***'Well, first of all, I think that there's pressure elsewhere and globally in the future for...that breeding can be done with plants, for example. There are great many different types of breeding needs caused by the changing environment and the fact that we need to increase food production, and of course the climate is a part of the changing environment, but through it, for example, the spread of plant diseases, the atlas keeps changing all the time, the pollinating insects, also spreading to wider areas and towards Finland, too, so we can think that we'll have new kind of pressure here during the next years, decades. ...and I don't know for how long, really, Europe can abstain from it, not exporting or importing, that everything should be processed through the most rigorous legislation, as transgenic plants ...in this sense, these economic losses are quite significant, because plant diseases alone make a big dent in this and economy, productivity, like, the quality of the infected plants is so bad that even if you could produce them, you couldn't really sell them.'*** [research representative]
>
> ***'You could think that something, like the potato that it's been bred for hotter conditions, but you can't necessarily bring it here, to Finland from somewhere, because we have a different length of the daylight and all that, so it wouldn't adapt to things here. So, even if it's done through traditional breeding, mutating a quality to be applicable in one place doesn't necessarily work in another geographic location. So, you can't be secure in thinking that we already have drought resistant, we already have heat resistant varieties, because I don't think it's certain, that the applicability would be good in other conditions, whatever they may be.'*** [research representative]

Especially in plant breeding, not using new genome editing techniques was considered a threat, because mutagenising, for example, northern cultivated plants or trees is slow using traditional breeding methods, if the climate conditions keep changing rapidly. The current, highly selected plants and the lack of diversity form a risk, if plant vitality decreases greatly through climate change. This may cause great crop losses and weaken self-sufficiency.

> ***'the challenges are so immense that there would be no sense in not using a technique that could help us move forward, it feels like sheer stupidity, to be honest, to exclude a plant breeding technique, even though it would get us to some good end result faster.'*** [company representative]
>
> ***'And if you can use genome editing elsewhere in the world, but not here, well then...in a way, it's like we get stopped, and suddenly we don't, if you compare this to driving a car, then we'd be using old diesel cars and can't move on to electric cars.'*** [farmer]

The benefits of the new genome editing techniques were considered especially to **be the ease of use, speed, and precision.** On the other hand, regulation and market expectations have a great influence on the emergence of applications. Strict regulation makes application too expensive for small and start-up companies. Furthermore, it was also stated in the interviews that developing and introducing plants produced by new genome editing techniques would not happen overnight if the legislation was to become more lenient. We should be prepared for this well in advance.

All in all, the economic significance of new genome editing techniques was considered great. It was estimated that if the use of the technologies were free, the economic value would amount to a 100 billion euros in a year. The genetic engineering market is estimated to grow from 500 million US dollars (2018) to a 1000 million dollars by the year 2023. It was deemed important to get more productive cultivated plants to the changing climate conditions. Among other things, the new genome editing techniques can improve disease resistance and tolerance of abiotic stress, enhance photosynthesis, and even expedite the replacement of fossil fuels. Additionally, genome editing can improve food quality. To illustrate, it can make fatty acid composition healthier and remove harmful or bad tasting compounds. These things were noted to even promote public health in the long run, as the usability of plant products improves.

> ***'stopping the increase of carbon dioxide is the goal, so if we can make, for example, wood products with a very long lifespan, then they will absorb carbon for a very long time. And of course, vegetation is very important in absorbing carbon dioxide in general, so if we can increase that, it will naturally influence the carbon dioxide in the atmosphere. So, in that sense, these are like, very kind and ecological.'*** [research representative]
>
> ***'if we encounter a situation, where we'd have to breed new varieties in a tight schedule, the kind that would survive in quickly changing conditions, then producing varieties by traditional breeding, which may take 10–20 years, is too slow, so using new breeding enhancing GM techniques in that sense might be necessary.'*** [research representative]
>
> ***'I believe that using these techniques could be the answer to these climate change and food resource issues. They aren't problems, they are, like, solutions to the problem.'*** [organisation representative]

5 Animal Breeding and New Genome Editing Techniques

5.1 Current State

In Finland, the utilisation of new genome editing techniques in the **breeding process of livestock** has not been started yet. The field is, however, being monitored with great interest. With the aim of understanding the effect of mutations on a cellular level, gene editing has been tested in cell lines for the needs of basic research.

> ***'they are used in the genetic research of domesticated animals, but the sperm or the embryo that we produce and sell to the Finnish agricultural entrepreneurs are not edited.'*** [breeding organisation representative]

Compared to plant breeding, animal breeding has several factors making the use of genome editing slow/difficult. Big livestock breeds slowly, and they have few offspring. The spreading of a certain quality to a breeding population from one or a few edited individuals takes generations and requires strict monitoring of the degree of inbreeding.

> ***'with the breeding of domesticated animals in the traditional sense, the numbers of animals are quite large, and you have to take care that the inbreeding doesn't climb in the population, and then, if you think that you produce an individual with great effort, which would otherwise be superior, and then it has a hornlessness or disease resistance gene, you simply can't use it too much on a population. Or can you make so many individuals that the idea of hereditary diversity gets actualised?'*** [breeding organisation representative]

The objective of genome editing of livestock could, in principle, be the improvement of the production traits of the animal, or the production of valuable proteins, for example, drugs or cells/tissue. Among the Nordic countries, Finland was a pioneer in gene transfer projects for domesticated animals. The projects were designed for medicine production. To illustrate, a genetically modified cow named Huomen was born in Kuopio university in 1993. It was meant to secrete the EPO hormone into milk. In fear of patent rights issues and harmful health effects, the transfer gene was not activated in the end. For some time, there were plans in Kuopio in the late 90's (FinnGene Oy/Pharming BV) to raise genetically modified cows from Holland for lactoferrin production, and to produce milk containing

lactoferrin. The enterprise fell through due to public protests (which we had far fewer in Finland compared to Holland) and the company bankruptcy.

The improvement of production traits with (expensive) genetic transfers was not regarded as profitable, since most economically significant traits are the result of the combined effects of several genes. Genome editing techniques have opened new prospects in the improvement of multifactorial production qualities. However, a better and more accurate understanding of the genome, gene function, and their interaction is required.

One aspect that often is related to gene transfers or genome editing of livestock (cow, lamb, pig) is cloning, especially nucleus transfer cloning. To illustrate, with the help of nucleus transfer, a selected, desired mutation edited in cell culture can be transferred to an embryo by using the nucleus. It is then to be implanted in the recipient. Nucleus transfer cloning carries a heightened risk of placenta or embryo deformity, or overgrowth of the offspring. Genome editing can also be carried out directly in a fertilised egg, which reduces cloning-related problems.

The breeding of insects as livestock is a fairly new concept. NGew genome editing techniques have been utilised in improving the disease resistance of the silkworm around the world. The utilisation of genome editing techniques for insects is limited to only a few species so far due to difficulties with the microinjection technique.

Non-livestock animals are under basic research with genome editing techniques in Finland, such as the *Drosophila* flies and the zebrafish, but they are not produced in Finland. For example, genome-edited mice are an everyday part of research in medicine. Also, some pets have been edited abroad for researching disease models of humans. With felines, the production of a hypoallergenic cat has been suggested and attempted. With pets, too, the ethical concerns call for serious contemplation before genome editing them can become approved by the public. Thus far, experiments of this kind have only been carried out in China. It is likely that new genome editing techniques are applied to pets abroad, but the Finnish people interviewed in the context of this study did not make such indications.

5.2 International Scope

As of now, genome-edited livestock are not commercially available anywhere. The only genetically modified livestock in commercial production is the rapidly growing AquAdvantage salmon, which has received a conditionally operating growth hormone gene from another species of fish. Bringing the product on the market took 25 years, which reflects the difficulties in animal-related (and environmental) risk assessment, and

license procedure. Despite the licenses, the opposition from public opinion can prevent the sales of products in practice. The first AquAdvantage salmon were about to arrive in the stores in the USA, but several retail chains refused to take them in for sale[75].

Aquaculture is one of the fastest growing areas of food production. There are high hopes relating to it. Traditional breeding of fish has been carried out for a relatively short period of time compared to other livestock. In this field, genome editing techniques are seen around the world as an opportunity with great potential. High offspring production, extracorporeal fertilisation, and the large size of roe eggs make fish editing especially easy and tempting. For research purposes, gene editing (CRISPR-Cas9) has been performed around the world on many salmon, carp, and other species of fish, as well as on oysters. Some of the targeted traits have been sterility, growth, and disease resistance. Sterility is important, so that the edited populations cannot mix with the wild populations. Among the genome-edited fish, one line of tilapias with edited growth qualities has been issued an exemption from GM regulation in Argentina[76].

For the approval of genetically modified animals in the EU, the applicant must publish the available analysis method for the identification of the animal line. Eurofins[77] has developed a DNA-based identification method for the genetically modified salmon. It may be challenging to implement similar identification methods for genome-edited animal products. Together with Finnish Food Authority, the Customs oversee monitoring importation in Finland.

> ***'As the Finnish representative of this European Network of GMO Laboratories… They are heavily debating how we are going to get our hands on these gene modified, both known and unknown, how they can be monitored, how their origin can be proved and so on. I mean, this discussion is very heated at the moment.'*** [official]

The earliest genome edits on livestock were carried out by utilising the TALEN-HDR method (transcription activator-like effector nucleases and homology-directed repair) combined with nucleus transfer cloning. The most famous example is the transfer of the cow polled quality (POLLED Allele) from beef cattle to dairy cattle. However, it should be noted that in this specific case, the transferred allele replicated, and therefore, plasmid segments used as a repair model also transferred into the genome. These changes

75 https://thecounter.org/americas-biggest-retailers-foodservice-companies-gmo-salmon-aquabounty/

76 https://www.fishfarmingexpert.com/article/aquabounty-gets-argentina-go-ahead-for-edited-tilapia/

77 Eurofins Gene Scan Technologies GmbH. A new kit for the detection of genetically modified salmon in food and feed. https://www.eurofins.de/kits-en/news/gmo-salmon-testing-kit/

were then also inherited by the next generation[78]. That being said, no side effects were identified in the edited animals.

The first genome-edited cattle are more than likely to enter the market in South America, at least in Brazil. In Brazil, the genome-edited animals do not require a specific GM permit, if they do not contain foreign recombinant DNA. Furthermore, in Brazil, the genome edits intended for production purposes are focused on better heat resistance. The CRISPR-Cas9 method has been implemented to edit a single pigment gene, so that the colour of the hair becomes lighter[79]. With the TALEN method, a gene of the prolactin receptor has been edited to thin the hair (Slick mutation). Slick is a mutation that occurs naturally only in the Criollo cattle from South America[80]. Currently, there is a desire to transfer that mutation to the more efficient western beef cattle (Angus), so that the cattle could be raised under local conditions[81]. To improve resistance to diseases (such as pneumonia, tuberculosis), genome editing has been applied in cattle. However, none of these edits have been taken to production.

In pigs, new genome editing techniques have been mostly focused on improving resistance to diseases[82]. The most promising examples from the practical point of view would be resistance to PRRS (porcine reproductive and respiratory disease) and resistance to African swine fever (ASF), produced through genome editing at the Roslin Institute in Scotland. Neither of these viruses exist in Finland as of now, although it is possible that they will spread due to climate change. In the editing of PRRS resistance, an attempt has been to edit the CD163 gene, through which the virus invades the cells. The AFS resistance has been implemented by editing the gene allele of a livestock pig to correspond to the disease-resistant RELA gene of a common warthog. In addition, the edits on pigs have also attempted to reduce the so-called boar taint, which is one of the reasons male pigs are castrated prematurely. However, as of now, none of these edits have been implemented in breeding.

If genome-edited livestock would be imported to Finland in the future, the most likely country of origin would be one with permissive legislation, such as China, Japan, the

78 Young AE, Mansour TA McNabb BR, Owen JR, Trott JF, Brown CT, Van Eenennaam AL.2019. Genomic and phenotypic analyses of six offspring of a genome-edited horn-less bull. Nature Biotechnology

79 https://www.newscientist.com/article/2256097-cattle-are-being-gene-edited-to-help-them-survive-climate-change/

80 Huson Hj, Kim ES Godfrey RW, et al. 2014.Genome-wide association study and ancestral origins of the slick-hair coat in tropically adapted cattle. Frontiers in genetics 5:101

81 Bellini J. This gene-edited calf could transform Brazil's beef industry. https://www.wsj.com/video/series/moving-upstream/this-gene-edited-calf-could-transform-brazil-beef-industry/D2D93B49-8251-405F-BC35-1E5C33FA08AF

82 Chris Proudfoot, Simon Lillico, Christine Tait-Burkard, Genome editing for dis-ease resistance in pigs and chickens, Animal Frontiers, Volume 9, Issue 3, July 2019, Pages 6–12, https://doi.org/10.1093/af/vfz013

United States, Argentina, Brazil, and Russia. Post-Brexit Britain is going to reconsider applying the GMO directive on genome editing. Because the Roslin Institute is a global forerunner in the genome editing of livestock, it can be assumed that they would also produce material for breeding.

If Finland would produce genome-edited domesticated animals, the Asian countries could be potential targets for their export. However, cattle are mainly exported as insemination doses, and currently, Finland does not have commercial semen production. For the most part, that takes place in Denmark.

> ***'where would that be headed, and when discussing exporting, I'm sure that currently, that place might be Asia.'*** [breeding organisation representative]
>
> ***'Faba does not produce the semen, rather, we are currently co-owners of VikingGenerics, who then own the bulls that produce the semen.'*** [breeding organization representative]

5.3 Future: Threats and Possibilities

Regarding animals, possible genome editing tools will probably continue to focus on **the improvement of animal health and welfare**. Reducing diseases improves production sustainability: by reducing the premature removing of animals, it is possible to increase resource efficiency and decrease emissions and the use of antibiotics.

> ***'And considering disease resistance, we have – there's a lot of information on – antibiotic resistance that seems to be discussed constantly, but we're out of options, so it might be possible that, for example, in animal production, genome editing would be exactly something that could be applied as well. You wouldn't need to use antibiotics, since the animals would already have better resistance to begin with, and the immune system would react much faster than it does now.'*** [producer organisation representative]

Genome editing influences the acceptability of animal production (e.g., the possibility of giving up chick culling, pig castration and cow polling), and it can prove useful in the future. Removing harmful alleles from elite lines through genome editing may prove feasible in some situations as well. With many animal species, identifying suitable targets for editing and understanding gene interaction is challenging. It is estimated that the next decade will continue to focus on basic research, considering both the development of methods and the defining of goals before we are truly ready for application.

> ***'There's currently a lot of discussion on domesticated animals regarding issues that breeding has caused for various species, and what comes to mind is that gene editing could be considered in solving these issues but, of course, that might not be around the corner just yet.'*** [veterinary medicine, researcher]

Furthermore, due to climate change, we might need animals that can withstand temperature variations in Finland as well.

> ***'so, in the future, we'll need resistant animals that are able to withstand these climatic conditions … for now, in Finland, we have that nice 20 degrees inside, but we might not be able to ensure that in the future, considering what's energy efficient and sustainable for the environment and nature, so I believe that in Finland, too … we should also consider the resilience of these animals and things like that, so that they wouldn't be so susceptible, if there's a heat wave…'*** [veterinary medicine, researcher]

As of now, compared with plant breeding, it is even more important to ensure that genome editing techniques used in animals are not linked to off-target or other effects that can prove harmful to the animal. In addition, the sought changes can also have unpredicted side effects. For example, if we inhibit the function of a cell surface receptor to prevent pathogens from entering the cell, we must first find out what other functions this protein has in cells.

> ***'thorough assessments to, for example, find out where these changes in the genome occur and whether they have any effects on (allergy) potential or on invasiveness and so on.'*** [an official]

During the planning stage of genome editing projects or gene transfers in animals, risks related to health and welfare must be considered. These aspects were not sufficiently considered with the first gene transfers in farm animals, and these gene transfers attracted major negativity due to the side effects that they caused. For example, transgenic pigs that were injected with cow or human genes that produce growth hormone had joint diseases, metabolic disorders, paralysis, and central nervous system problems[83].

> ***'so, if we want to do things like genome editing in animals, we definitely need to have strict ethical discussions'*** [company representative]

83 Pursel VG, Hammer RE, Bolt DJ, Palmiter RD, Brinster RL. Integration, expression and germ-line transmission of growth-related genes in pigs. J Reprod Fertil Suppl. 1990;41:77–87. PMID: 2213718.

> ***'so are the techniques (that precise) … Is it still possible there could be some changes that could have an effect on animal health or development, for example? But a bio-threat sounds so massive, so… there's something… or like this feeling that can this be so simple? That we achieve just that one thing? It might turn out that we've had a debilitating effect on something else, if it's not that precise or if we aren't that familiar with the effects of the genome after all, and… then it turns out like that, because there is gene interaction and so on, so it can turn out… I wonder what kind of a mutant cow we might create?'*** [breeding society representative]

In the future, the type of editing might also influence the acceptability (and possible regulation) of genome editing in animals. Considering variations that occur in nature, converting one or a few bases can be more easily accepted than changes that are probably not present in nature.

6 Medical Science and New Genome Editing Techniques

6.1 Current State

In addition to plant breeding, genome editing is also common in basic **medical research**. Overall, genetic engineering has already been used in medical research for over 40 years. During the past few years, we have seen some targeted genome editing especially in creating animal and cell models for diseases more rapidly and accurately. With the help of animal and cell models, we can examine human diseases and find and develop pharmaceuticals. For example, there are currently genome-edited mice with high cholesterol. With the help of these mouse models, we can examine how prodrugs and drugs can be used to treat high cholesterol.

We are quite close to commercial applications in medical research and development. With new genome editing techniques, we can edit gene defects of somatic cells in individuals. Many of the medicines that are under development are biological ATMPs (Advanced Therapy Medicinal Products). Their function is based on adding a therapeutically useful gene to a specific location or inhibiting harmful gene expression in a specific tissue. Currently, these types of treatments that are focused on gene therapy target rare diseases and are carried out at an individual level, but they can already be considered commercial to some degree.

> ***'CRISPR-Cas and zinc finger nucleases and TALEN nucleases and… others, so there are different technologies we can use, as you know, to edit the genome in a very targeted way, so that the editing is done in a selected location. And that would, of course, be… an optimal way to treat, for example, a hereditary disease that entails a faulty gene with defective gene expression that causes this serious, disabling disease that might lead to an untimely death. ---- specific, targeted genome editing techniques aren't yet that developed that we could apply them in clinical use in the next few years.'*** [company representative]

Under the Gene Technology Act, the supervisory authority for medical science is the Finnish Medicines Agency FIMEA, which does not systematically collect data regarding the extent of the use of new genome editing techniques. In addition, implementing a technique does not usually require submitting a new notification referred to in the Gene Technology Act to the Board for Gene Technology that acts as the competent authority, if

the previous notification on contained use already includes vector organisms used in the editing (e.g., lentivirus), and the recipient and donor organisms and the nature of their use will not significantly change due to the implementation of new techniques.

Genome editing with CRISPR-Cas9-based techniques that aims for animal testing in medical science is carried out and offered as a service by at least one Finnish laboratory animal centre according to information on their website. According to the interviews, new cellular components or animal models that are usually used in research are purchased from abroad. The Board for Gene Technology, which operates in conjunction with the Ministry of Social Affairs and Health, has received information that there has been use of Arabidopsis (thale cress), zebrafish and Drosophila (fruit flies) edited with the CRISPR-Cas9 technique.

According to FIMEA, based on data from literature, CRISPR-Cas9-based techniques have revolutionised genome editing in eukaryotes, but they have had far less impact on genome editing in prokaryotes or viruses, since their genomes can be edited in a targeted way with previous techniques as well.

FIMEA has no knowledge of CRISPR-Cas9-based techniques being used in Finland in, for example, creating genetically modified cells for therapeutic use. However, according to the interviews, Finns are definitely a part of the international research that aims to improve gene therapy.

Both large and small companies as well as the academic world are involved in this development in medical science.

> ***'And I must say that, at the moment, no one – not even large multinational pharmaceutical companies are dominating or controlling this. It's still very much in the hands of academic work and academic and pharmaceutical companies and small SMEs whether this will prove useful.'*** [medical researcher]

However, research and development in medical science utilising new genome editing techniques is hindered in Europe by a stricter legislation compared to other parts of the world. For example, in the United States, it is possible to perform more straightforward drug trials than it is in Europe.

> ***'…in Europe, we even have to perform preclinical animal testing with a pure product produced in a pharmaceutical company, a product that requires millions, and this is an example of something we're constantly falling behind on. In the US, they can do fast screenings with even just a few dozen volunteers to see if they work, and they can choose those they should advance faster, but Europeans***

> ***have to constantly struggle with the unpleasant fact that we need to have a pharmaceutical company that has a licence for the manufacture of products and that even genetic medicine used in the final phase of animal testing needs to be manufactured with massive costs…'*** [medical researcher]
>
> ***'But over there [USA], it's easier to push commercial products through and at least carry out the research. Meanwhile, we can't even… we don't get any investments, since the companies… even if we had a good product that someone could develop into a commercial success, it would be difficult to do the research here, because if you get it patented in the EU… or you can't sell it in the EU. So, they'd rather do the research elsewhere, too, somewhere where it's easier.'*** [medical researcher]

6.2 International Scope

The activities are strongly international, and Finland is at the forefront. There are great financial and export-related possibilities for medical products that affect gene expression. Finland is a leading country particularly in gene therapy along with the United States and the United Kingdom. Germany, France, and Japan, on the other hand, are a little behind with their expertise. Of the Asian countries, China is quite intriguing and clearly at the forefront of genetic engineering.

> ***'The way I see it, the situation in Finland is great. First of all, we've had research on gene transfer since the early '90s, and Finland is one of the world leaders in this expertise.'*** [company representative]

6.3 Future: Threats and Possibilities

The prospects of genome editing in medical science are very promising. The financial benefits that can be achieved with the technology are substantial as well. It is very likely that in the future, we will have medicines that have been manufactured utilising genome editing techniques and a possibility to repair faulty genes that cause hereditary diseases. At the moment, only those treatment techniques based on genome editing that are used in specialised health care will likely be implemented in public health.

> ***'…this expertise in genomes will no doubt result in us all having a chip in our neck with information about our genes that can affect drug metabolism or cause a risk for a disease, and doctors and other health care personnel will utilise that in, for***

> ***example, prescribing suitable medication, so that they won't do anything that would likely cause side effects.'*** [medical researcher]
>
> ***'especially regarding the treatment of difficult hereditary diseases, but also, for example, regarding some forms of cancer that are caused by certain mutations. We'll definitely have some targeted treatments, effective treatments for difficult diseases.'*** [medical researcher]
>
> ***'to overestimate the rate that these new technologies can be implemented, but on the other hand, underestimate their effects in the long run… in practice. ---- a significant transformation in medical science. But what the time frame with that is, if it's 10 years from now or 20 or 30, well, that I can't say for sure.'*** [company representative]

From the perspective of medicines agencies, genome editing currently entails no threats to the population. In fact, a large threat regarding the technologies could result from some harmful procedures that would cause threat associations towards technologies which would turn off the money taps that provide funding for new genome editing techniques. This type of a threat could be increased by careless research, such as editing the human germline, or by creating commercial applications too fast, which could result in, for example, vaccines that cause long-term and irreversible damage. However, there is a consensus among researchers that a responsible researcher will not edit human gametes or allow unlicenced selling of products in the market.

The possibility of an actual bio-threat through the release of genome-edited material into nature is extremely small. The use of medical, genome-edited matter is contained in a way that the matter is not handled outside or in nature.

> ***'…medical treatments and things like that are made – it's contained use in hospitals or in operating rooms, and the discarded matter can be handled, inactivated, so that the risk of an accidental release into nature is very small, so as a comparison, there are all these difficult bacterial diseases, Ebola, plague, tuberculosis, that can be analysed in hospitals, treated and contained. So that the medical science doesn't suffer from this accidental spread into nature and the risk assessments and regulation and additional testing that it would cause, so in a way (we're) perhaps in a somewhat better situation.'*** [medical researcher]

Terrorism and biological warfare are threats that should be considered, and the danger level can increase with the use of these new genome editing techniques. However, this type of misuse requires high expertise, and this somewhat contains the threat. In addition, the complexity of the biological systems in part protects us from that threat as well.

> ***'…so, these genome techniques are pretty difficult to control, so for now, they are handled by researchers with high ethics and morals. But time will tell, if the financial aspects or something will become more important … I don't think the genome is something to be afraid of, since it works in a certain way and limits itself as well, and evolution is very effective, and there are many aspects that ensure that this type of a system that has all its eggs in one basket won't usually get very far.'*** [medical researcher]

7 Research and Education Requirements

Based on the interviews, it appears that new genome editing techniques are currently used only in the plant and medical sciences, as well as for research and education in molecular biology. The interviews conveyed that funding should be directed to genome editing techniques, which have great potential. According to the interviews with research funders, basic research involving genome editing is already reasonably well funded in Finland. However, projects in applied research are in practice not funded.

> ***'the number of funding applications for projects that use genome editing methods has increased, and projects that have already received funding indicate how the number of these projects that use new editing techniques has grown during the past few years. And well, I also looked at the number of projects that have received funding from the Academy of Finland and the number of Finnish project publications in general, and those have also increased during the past few years. I looked at the data from the past five years, and in fact, we had an intern last spring, who I asked to look into this a little, and during the past five years, there's been 23 million euros worth of funding for altogether 58 research projects that have, one way or another, used these genome editing techniques. And most of these are just basic research.'*** [representative from research funding]
>
> ***'so, it would be good to do at least a superficial examination of these kind of things in food technology, even though they don't really make experts for that ---- a kind of an education that these are very potential methods and that you shouldn't believe the kind of propaganda that may be – or that you might see in media coverage that gene editing techniques are somehow bad.'*** [company representative]
>
> ***'if we educate them for the future, genome editing techniques should be included. I mean these new genome editing techniques should absolutely be included pretty strongly in the degree programme.'*** [organisation representative]

Regulated import of organisms that are created with genome editing techniques and used in research and education can prove complicated based on the interviews, because official liabilities are unclear. Genome-edited organisms, whose genetic elements are purchased from abroad, are used in research and education in molecular biology. Key organisms

currently studied in molecular biology are the model plant Arabidopsis, barley, zebrafish, and mice. In addition, genetic elements of genome-edited organisms used in medical science are also purchased from abroad these days.

> ***'but also, any time I've had to procure or submit notifications to the Board for Gene Technology, it's been difficult, because it's hard to find them, to find information on how these notifications are made, and when you need a licence and when you send in a notification, and I think this has really been difficult. And now we have this, which might be mentioned next as well, that when you order materials, it really is difficult to find information anywhere on how you should go about ordering genetically modified material from the US, for example, so who regulates it and who you should submit a notification to and who is allowed to do what, so like this bureaucracy is definitely hard… So, I think this is what we're mostly lacking, I'd say, finding information on what you can and cannot do and how you should do it.'*** [research representative]

The interviewed experts clearly stated that to increase the public's knowledge and understanding, genome editing techniques should at least be covered in secondary education, not only in universities. It should be taken into consideration in curricula that in the future, the public needs to be aware of concepts related to biology and genome editing to a degree where they would be able to have general knowledge of the applications of genome editing techniques and to participate in discussions regarding their use.

> ***'Ignorance is a bliss, but well… I'd say that if you don't know enough, you oppose easily. I think that if you don't know about these genome editing techniques and we don't have open discussions on them, you'll probably get a little scared, like what is this.'*** [farmer]
>
> ***'it would probably be important to talk about these things. We should introduce these new opportunities in an impartial and neutral way, so people would understand what it's all about. We could probably then reduce some of the fears.'*** [company representative]

Ethics, legislation, and critical thinking should also be taught more in universities. In addition, genome editing should be covered more in agricultural studies. Especially in describing plant breeding methods, transparency should be increased for farmers to understand what they are growing. GM education should also be added regarding food supply chains and food technology. Ethical perspectives, attitudes, and method descriptions would be important aspects to comprehend.

'at a university: gene editing techniques would be taught hands-on in labs as well, so not only in lectures, and meanwhile, you could also go over ethical aspects and these gene technology legal acts that are applied in Finland and Europe.' [research representative]

'how secondary school graduates answer, like I've always been even a little surprised how well they know things and are aware of these CRISPR-Cas techniques, for example' [research representative]

'Decisions aren't based on knowledge… This is based on the fact that people don't know, so they're worried about things, like we are all worried about things we don't understand. So, it's a big, big worry that the baby would be thrown out with the bathwater, if you don't understand what it's all about. And since we live in a democracy, if enough people are worried, our decision-makers are afraid to make decisions, since they wouldn't then be elected in the next elections. That's how it works.' [research representative]

8 Possibilities of New Genome Editing Techniques from the Perspectives of Finnish Business, Import, and Export

Considering overall imports and exports, the largest group of products imported into Finland includes medicines and pharmaceuticals. This trend is expected to continue, and since these fields are already prepared to utilise the new genome editing techniques, it is also likely that, in the future, medical products will be the largest group imported into Finland that were developed or produced with genome editing. Regarding exports, the largest group of products is clearly paper and paperboard. The forest industry plays a central role in the manufacture of products in this group. The possibilities of new genome editing techniques in plant and tree breeding, especially in making wood production more effective, are significant in this development.

Figure 6 portrays Finnish imports and exports regarding products, whose manufacture could possibly benefit from genome editing tools. The data has been collected from the 2020 statistics[84].

84 The statistics search was carried out by Mika Naumanen from VTT.

Figure 6. Finnish imports ("Tuonti") and exports ("Vienti") regarding products, whose manufacture could possibly benefit from new genome editing techniques, from the 2020 statistics. Largest exports are "Paperi ja pahvi sekä tuottet niistä", paper, cardboard, and products therefrom.

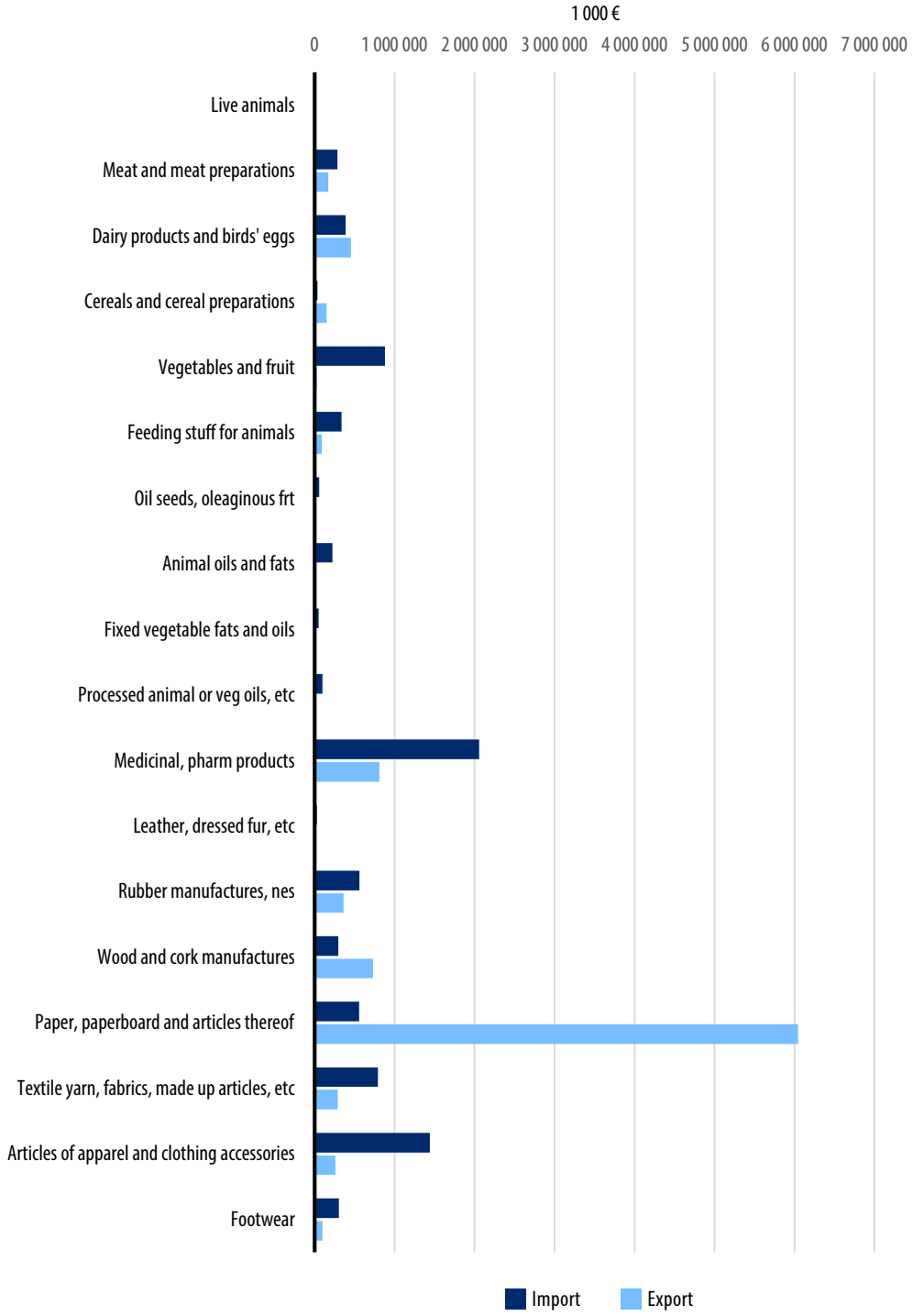


Figure 7, on the other hand, specifies examples of the imported and exported food products for which plant species, according to published research, genome editing techniques have been applied in research (cf. Alan Schulman Figure 5 in Chapter 4).

In this group, the most imported product into Finland is clearly fruit. This could result in foodstuffs developed through genome editing techniques being imported into Finland to an increasing degree in the future.

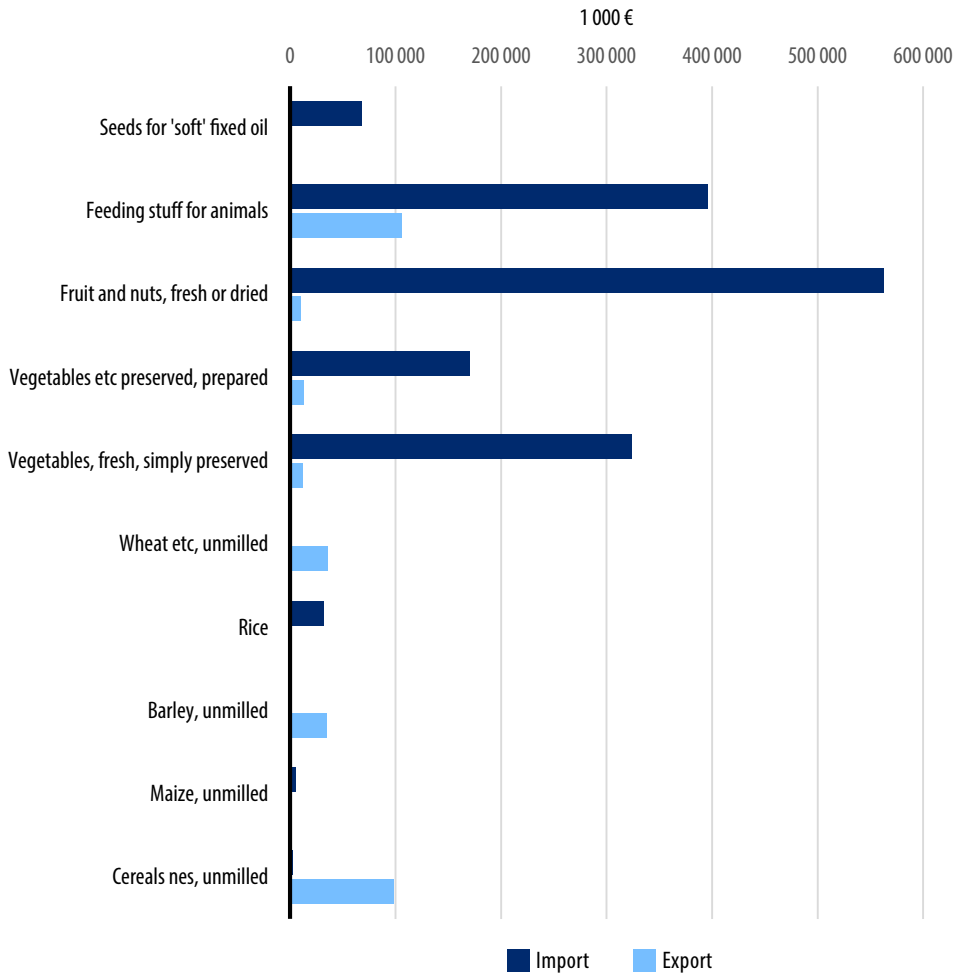
In the EU countries, genome editing has been utilised in basic research of cereal crops mostly for barley. Likewise, the major cereal export from Finland is barley malt and likely will be in the future. Malting barley, on the other hand, is Finland's largest grain export product. It is exported from Finland at about 120,000 tons per year[85]. Currently, the price of malting barley is 174 € / tn[86], so the value of total exports per year is about 20 million €. Moreover, much of the north-European malting industry is under Finnish ownership, affecting variety choice. Biomass derived from trees is a major export product as wood, cardboard, and paper. Hence, regarding export, genome editing in barley and trees seems likely future targets. In Finland, the growth in production of oat and protein crops (e.g. faba bean) for vegan food products is increasing, and have export potential. Genome editing of these plants is therefore likely to be seen in the future.

85 VYR Vilja-alan yhteistyöryhmä: https://www.vyr.fi/mallasohran-viljelyopas/mallasohran-tuotanto/

86 VYR Vilja-alan yhteistyöryhmä: https://www.vyr.fi/mallasohran-viljelyopas/mallasohran-tuotanto/

Figure 7. Some examples of exports and imports from and into Finland of products and plant species. According to the litterature and reports these plant species have been included in the studies related to new genome editing techniques. (cf. Figure 5).

Taloustutkimus carried out a questionnaire survey aimed especially at companies. It



provided a limited sample (n=44 respondents from 43 different companies) of the overall picture of the current and future demand of companies in different lines of business for genome editing techniques. The themes in this survey included the scope of use for genome editing techniques, the level of expertise regarding their utilisation, and the development of imports and exports based on genome editing. The survey showed that companies operating in various fields believe that the use of genome editing will increase in various lines of business.

A little over third (39%) of the companies that participated in the survey currently use genome editing techniques[88] or raw materials or products produced utilising them. Currently, the share of companies' revenue derived from genome edited products is quite small, but the survey reached a few respondents whose companies had clearly directed themselves to this sector. However, a more detailed account of these companies cannot be acquired due to the anonymisation of the survey.

Companies (n=27) that are not currently utilising genome editing techniques, raw materials or products produced thereby believe that the utilisation of these techniques will increase in their companies. All respondents believe that the importance of genome editing will increase in the future – none of the respondents disagreed in this matter. Expertise, the development of technology and legislation, and cost-efficiency were mentioned as examples of factors that would expedite this change.

The lack of utilisation of genome editing is currently justified by there being no need for it yet or it not fitting the company's business model. Even if the use of these techniques is not currently relevant, most of these companies (70%) believe that it will be relevant during the next ten years – every fourth (26%) expects it to begin perhaps even within two years. Views on the use of genome editing techniques in the respondents' own line of business in the next five years were also very positive. A great majority (89%) believes that it will increase in their line of business at least to some degree.

Legislation and attitudes were mentioned most often as factors hindering the implementation of genome editing. More than half (57%) of all the companies that participated in the survey currently lack sufficient tools, expertise, and know-how on the application of these techniques. The respondents see that the biggest drawbacks include the lack of know-how and the fact that the company itself does not use or apply the techniques.

Consequently, nearly all the companies that participated in the survey have international operations. Approximately every third (32%) has imports that come from multiple countries or market areas – mostly from the EU and the United States, as well as the Nordic countries. The imports include medicines, feed components, gene therapy, raw materials for diagnostics industry, disease-free plants[87], bull embryos or sperm, and vitamins and enzymes. More than two out of five (42%) were unable to say whether the company's use of genome editing techniques or a demand for them was based on imports. Along

87 Most likely for contained use, since there are no disease-free, genetically modified plants or plants modified with new genome editing techniques in the EU market.

with imports, exports include multiple countries or market areas as well – the largest being the EU area.

Company representatives mentioned many views on what were considered critical matters, in which the companies would need or want help from legislators or supervisory authorities. Many highlighted the need for clarifying and updating the legislation – regarding imports and exports as well. Furthermore, companies hope for clearer guidelines. They are unwilling to risk safety, but they want to eliminate unnecessary bureaucracy. They also hope for a change in public attitudes and more freedom in research and product development. In addition, they hope for increase in dialogue and other cooperation, so that the knowledge of legislators and supervisory authorities on the matter would increase. Similar hopes were stated regarding the operations of the Ministry of Social Affairs and Health.

Furthermore, an overarching message for both officials and legislators was that genome editing techniques will be a part of everyday life in the future, and that we should take part in their development, so that Finland can stay competitive with other countries. There is a lot of uncertainty and negativity on the subject in Finland. Companies believe that it would be important that along with emphasising risks, knowing how to highlight the advantages achieved with genome editing could be crucial: resistance to disease, quality and good crops, treatment of serious illnesses and many other qualities that can be improved safely and cost-efficiently with genome editing.

Similar messages regarding the field's prospects were also brought up in the project's stakeholder workshop that included participants from the corporate world as well. Dialogue with decision-makers and the development of regulations were highlighted, and consumers were considered as important gatekeepers for the field's development. The workshop emphasised the need for decision-making based on knowledge and facts. Furthermore, in addition to risks related to the utilisation of genome editing techniques and decision-making on the field, the participants hoped for discussions on the possibilities created by the technology. This would be a change from the current situation, where decisions are mainly influenced by risk assessments. Considering the future, genome editing was considered applicable especially for improving the quality of life, reducing environmental problems, and developing innovations. Participants considered consumer attitudes essential for the future of the field, and they hoped for more support and measures for this as well through, for example, providing illustrations and everyday examples.

9 Development Paths of Genome Editing: Scenarios

9.1 Background

The scenario analysis of this research project focused on the future of the utilisation of new genome editing techniques, and on the possible development paths in the field of plant breeding.

We decided on an industry-specific scope, since a combined analysis using the scenario method for different lines of business was considered problematic. This is because different lines of business are in rather different stages of development regarding the use of the new genome editing techniques, and the variables used in the analysis are not equivalent or as essential for all industries.

Plant breeding and agriculture were considered the most suitable industries, since for them, the effect of legislative developments was considered the most significant as they affect, for example, the risk assessments required in the industry and, finally, business developments. Considering medical science and animal breeding, the analysis is more strongly related to studying ethical questions than in plant breeding, and it is more difficult to do that objectively.

In scenario-building, a report on genome editing by the Dutch Rathenau Instituut[88], a discussion paper of the Norwegian Biotechnology Advisory Board[89] and All European Academies ALLEA's outlines of the future possibilities regarding EU regulations[90] were utilised, among other sources.

88 Habets, M., Hove, L. van and R. van Est (2019). Genome editing in plants and crops – Towards a modern biotechnology policy focused on differences in risks and broader considerations. The Hague: Rathenau Instituut

89 The Norwegian Biotechnology Advisory Board (Bioteknologirådet). The Gene Technology Act – Invitation to Public Debate. 2018.

90 ALLEA (2020) lead authors: Dima, O.; Bocken H.; Custers, R.; Inze, D.; Puigdomenech, P.; Genome Editing for Crop Improvement. Symposium summary. Berlin.

This scenario analysis was especially focused on one research question:

- Is the use/non-use of these techniques connected to the national preparation for other types of threats (e.g., climate change, food security)?

9.2 Description of the Scenario Method

Scenarios are tools for making predictions and for strategic thinking. A scenario analysis does not aim to create a more probable picture of the future, but rather conditions for strategic and responsible actions in the present moment.

Scenarios assist in picturing the possibilities of alternative outcomes and through those, it is possible to structure continuities and discontinuities that are important for operation. With the help of scenarios, it is possible to weigh the effects of different development paths and to prepare for them.

The stages of the scenario analysis carried out in this study were:

- Analysis of the operational environment: recognising the variables that are important for the subject area (uncertainty factors, continuities, and discontinuities). This stage included interviews with experts, a questionnaire survey, a stakeholder workshop, and a literature review.
- Creating a futures table: choosing the most relevant variables to be included in the study. These variables will be examined using the futures table. This is a table in which the column headings have the selected variables, and the columns contain the possible values for these variables.
- Future states: the selected values from the futures table. Creating a static view on a specific future state.
- Scenario paths: plausible explanations on how to achieve or end up at a specific future state.

9.3 Scenarios

We will introduce three different scenarios that significantly differ from one another regarding how the legislation on genetic engineering and the regulation of the new genome editing techniques are developed in the EU area, and what indirect effects this has on the development of public attitudes and business. The scenarios are named as follows:

Just in Case: The development of regulation is directed by the minimisation of risks. Strict regulation and significant obligations, such as risk assessment, prevent irreversible ecological risks from being realised, but at the same time, they limit the development and application of genome editing techniques.

Growth from Sustainability: The development of regulation is directed by opportunities. Deregulation enables new and experimental business models and the development of various new innovations and solutions.

Data-based Decision-making: The development of regulation is directed by the promotion of fair development. The purpose of multilevel regulation is to ensure diverse observation of the effects of genome editing as well as balanced distribution of its benefits.

9.3.1 Futures Table

Figure 8. Futures table with values of three different future states in plant breeding highlighted with different colours.

Regulation of Genetic Engineering in the EU	Interpretation of New Genome Editing Techniques in the Genetic Engineering Legislation	Consumer's Predominant Attitude towards the New Genome Editing Techniques	Applications of the New Genome Editing Techniques	Development of the Field of Genome Editing Focused on
Centred on the technique and/or technology	Equated with GM technique	Positive	Strongly centred and licensed	Maximising the benefits
Centred on the end product	Positive towards the new genome editing techniques	Nuanced: acknowledges the context of the field and of the application	Factually and genuinely available for all users	Minimising the risks
Multi-level hybrid model	Distinguished from GM technique	Sceptical	Determined according to the estimated broader impacts	

Just in Case | **Growth from Sustainability** | **Data-based Decision-making**

9.3.2 Just in Case

Future State 2030:

In 2030, new genome editing techniques will continue to be equated with genetic modification techniques (GM techniques). Behind this equation is the precautionary principle that controls the regulation of genetic engineering and that is used to avoid

potential irreversible and harmful consequences of genetic engineering to nature and humankind.

Plant varieties created with genome editing techniques are included in the GMO directive, and a lengthy risk assessment as well as strict labelling and monitoring are required to allow them into the market. Therefore, the marketing of genome-edited varieties is difficult and expensive. The minor commercial applications of new genome editing techniques in Europe are mainly centred in large multinational companies.

The EU stance hinders international trade, since the EU regulations state that the labelling obligation regarding genetic engineering falls to the producers of agricultural and food products created with new genome editing techniques that are brought into the Union. Because of this obligation, trade relations with countries that are unable to meet these labelling requirements have suffered setbacks. This benefits the traditional agriculture and producers in the EU area, whose position is secured at the cost of new methods of production.

Consumers and citizens in the EU area have reserved and sceptical attitudes towards genetically modified food because they see risks in genetic engineering techniques. Consumers prefer products of conventional farming and value organic farming. Farmers focus on producing and marketing products that are considered ecological and natural.

Scenario path 2021–2030:

Table 1. An imagined scenario path towards the future state 'Just in Case' that shows how business, regulation and public attitudes will develop during the next 10 years.

	2021	2025	2030
Business (EU)	Business development is hindered by uncertainty of regulation. Company investments remain low. This is due to companies' views on consumer attitudes towards products produced by genome editing. Due to the strict obligations that result from regulation, the development and potential applications of genome editing are possible mostly for large multinational companies.	Business is increasingly centred in larger companies. Demand for products created with new genome editing techniques remains low in the European single market, but global demand increases, since regulations are less strict outside the EU (especially in North America and China).	Global demand for products produced by genome editing has considerably increased regardless of the EU's sphere of operation, and the companies operating according to the EU rules have "fallen by the wayside". Top-level expertise in the field is clustered in North America and China which further reduces EU's competitive strength in the field.
Regulation and Public Attitudes	**Regulation:** The 2018 CJEU ruling equated genome editing with GM techniques, which stirs controversy and causes uncertainties regarding genome editing. **Public attitudes:** Genome editing techniques are mainly discussed among experts, and products created with genetic modification and genome editing techniques are not always distinguished in public discussions. In general, attitudes towards genetic engineering are cautiously doubtful.	**Regulation:** There is no room for genome editing in the regulators' agenda, since acute challenges, such as energy transition, divert attention and consume political capital. **Public attitudes:** Something inexplicable regarding GMO matters is said to have happened outside the EU, and this results in a butterfly effect of fake news. This both reinforces GMO's notoriety and results in pessimistic views on genome editing in the EU area, as all genetic engineering is seen as a whole in public discussions.	**Regulation:** Genome editing has been disregarded in political discussions, and its regulation is not actively developed. **Public attitudes:** Genome editing has remained a theme outside the mainstream, and there is not enough public discussion. People are rather uninterested in genome editing, and when the subject comes up in discussions, people feel doubtful towards it. All genetic engineering and its application areas are seen as a whole.

9.3.3 Growth from Sustainability

Future state 2030:

In the year 2030, genetic engineering legislation is focused on the end product, which means that it is based on evaluations of the varieties' and products' qualities. In addition to the traditional mutation breeding, giving up strict, technology-based risk evaluations has made genome editing applications possible, together with freer application of transgenic techniques. This creates opportunities for various plant breeding and agricultural enterprises as well as for research institutes to bring products created by genome editing as well as with genetic engineering to the market. In addition, regulation focusing on the end product creates business opportunities for various start-ups and SMEs.

The massive investments by the EU in the fight against climate change and supporting sustainability research and business development have been a significant driver for development. Improving food security is one of the main goals of the EU, and it is widely being improved by genome editing and gene transfer techniques. By applying genome editing, it is possible to improve yields as well as create varieties that are more resistant to diseases, drought, and other environmental challenges.

Public communication regarding genome editing successfully highlights the techniques as important tools in the fight against climate change as well as in reducing our ecological footprint and solving the food crisis. In public discussion, genome editing techniques are equated with safe plant breeding methods, which causes consumers to view products manufactured with genome editing as quite natural. Consumers also appreciate new versatile varieties and food products created with the techniques. However, regulation focusing on the end product removes labelling obligations from all genetically engineered products, which, according to some, reduces the consumers' freedom of choice when making decisions regarding purchasing groceries.

Scenario path 2021–2030:

Table 2. An imagined scenario path towards the future state "Growth from Sustainability", in which it is described how business, regulation and attitudes will develop in the following 10 years.

	2021	2025	2030
Business (EU)	Business development is slowed down by the uncertainty of regulation. Corporate investments remain low. This is caused by the idea companies have of the consumers' attitudes towards products made using genome editing techniques. Developing genome editing and its potential application is only possible for large, multinational companies due to the strict responsibilities caused by regulation.	Food production is stalled because of climate change. An acute shock, comparable to the Covid-19 pandemic, has happened, after which a significant harvest was spoiled, and the local and indirect effects are widely discussed in the news. This dramatically increases the demand for gene technology, with which food production can become more sustainable and resource efficient. The number of investments increases significantly, especially for new genome editing techniques.	The business environment in the EU has become more like those of China and North America. The business environment of EU begins to attract new companies and experts. Due to a high level of demand, new genome editing techniques are being developed and applied widely in the EU by many different companies.

	2021	2025	2030
Regulation and Public Attitudes	**Regulation:** In 2018, the Court of Justice of the European Union equated the new genome editing techniques with GM techniques, which causes disputes and ambiguities regarding genome editing. **Public attitudes:** Discussion on genome editing techniques is held amongst experts, and in public discussion, there is not always a distinction between genetically modified products and products created with genome editing. In general, the approach to genetic techniques is cautiously sceptical.	**Regulation:** Political pressure to decrease regulation increases suddenly. All measures will be taken into use and we will join the global mainstream regarding regulation and focus restrictions on the end product. **Public attitudes:** The combined effects of the climate change and population growth appears on the consumers' agenda widely. People are not ready to give up and change their diet. Instead, there is support for innovative and technological solutions that make it possible to be more resource efficient in the current food production system.	**Regulation:** The regulatory requirements for risk assessment have decreased, and instead of technique, regulation is focused on the qualities of the end product. **Public attitudes:** The carbon footprint of products made by new genome editing techniques is seen as a great success story, and the attention is no longer paid only to outdated information regarding the risks of GM techniques. People are proud of the EU for solving the food crisis springing from climate change.

9.3.4 Data-Based Decision-Making

Future state 2030:

In the year 2030, attempts are made to utilise new genome editing techniques in the most balanced and fair way possible. The new multilevel genetic engineering legislation of the EU is based on assessment regarding the degree of change achieved in the qualities of organisms as a result of genome editing and imposes regulatory obligations accordingly. This facilitates the legislative position and application of genome editing techniques but continues to impose restrictions on genetically modified (GMO) products.

In addition, the multilevel regulation by the EU pays attention to the principles of wider social sustainability by evaluating the societal effects of genome editing on food security, the position of vulnerable groups, and consumers' freedom of choice. Multilevel regulation facilitates differential product labelling, which in turn promotes customers' freedom of choice.

Public communication and discussion regarding genome editing is versatile and nuanced. Different genetic engineering techniques and the context of their application and possible consequences are clearly distinguished. In public discussion, more attention is paid to the long-term effects of genetic engineering on global food security, economic inequality, and lifestyles as well as to its effects on the vitality of the countryside and of agriculture.

The citizens and consumers want genome editing techniques to be applied as fairly and justly as possible. Thus, commercialising genome editing requires extra attention on the values and responsibilities of the parties applying the technique.

Scenario path 2021–2030:

Table 3. An imagined scenario path towards the future state "Data-Based Decision-Making", where it is described how business, regulation and attitudes will develop in the following 10 years.

	2021	2025	2030
Business (EU)	Business development is slowed down by the uncertainty of regulation. Corporate investments remain low. This is caused by the idea companies have of the consumers' attitudes towards products made by genome editing. Developing genome editing and its potential applications is only possible for large, multinational companies due to the strict responsibilities caused by regulation.	The growing interest of public authorities in developing industry and business and in increasing joint interaction is seen as a promising sign, which decreases the interest of companies in moving out of the EU. Investments remain moderate, but more experts are committing to genome editing due to the development of a positive operating environment.	In the EU area, there is a strong specialisation in products produced with genome editing that reflect European values. An ecosystem consisting of smaller and more specialised operators has been formed around the genome editing business, serving increasingly aware and demanding consumers. Operators also work together with several developing countries.

	2021	2025	2030
Regulation and Public Attitudes	**Regulation:** In 2018, the Court of Justice of the European Union equated the new genome editing technologies with GM techniques, which caused disputes and ambiguities regarding the genome editing techniques. **Public attitudes:** Discussion regarding genome editing techniques is held amongst experts, and in public discussion, there is not always a distinction between genetically modified products and products created with genome editing. In general, the approach to genetic techniques is cautiously sceptical.	**Regulation:** The development of regulation is guided by the will to promote fair and sustainable development. The need for dialogue with the applying actors is seen as critical. Positive experiences increase the will to expand discussion outside Finland. The discussion between public authorities and the applying actors on the level of Nordic countries is started at Finland's initiative. The joint message of the Nordic countries to the EU is well received and is considered to improve the position of the EU as a valued leader regarding genetic engineering. The development of regulation in the EU area will be initiated with determination. **Public attitudes:** Interest in the utilisation of new genome editing techniques increases slowly after the well-structured communication about it starts reaching consumers. The development of attitudes starts to shift from either-or thinking to a more versatile direction.	**Regulation:** The enablers of the responsible application of genome editing are: 1) new complex legislation focusing on the assessment of the degree of change achieved in the qualities of organisms as a result of genetic editing and their various effects, and 2) the functioning dialogue between the public administration and the applying operators. **Public attitudes:** Consumers understand the naturalness and possibilities of the products created by new genome editing techniques and can distinguish them from GMOs.

10 The Current State and Future of New Genome Editing Techniques

Currently, the utilisation of the new genome editing techniques has focused on research, especially basic research. Use of the techniques in the research and development of end products is rare, but there is interest in all sectors covered by this report, i.e., plant breeding, livestock breeding, and medicine.

In Finland, plants, microbes and algae with edited genes are already being used in plant science research; they are also being produced. In research, the effect of various genes on complex phenomena occurring in plants is being investigated using genome editing, including development and growth as well as biosynthetic pathways. Efforts to increase resistance to drought and disease and to improve quality traits are underway by genome editing of genes with major effects. However, incremental crop improvement breeding will nevertheless continue by selection of the best combinations of the many genes each offering quantitative traits. In the future, with the help of genome editing, there will be an increasing number of opportunities to enhance photosynthesis, produce biostimulants, improve food quality, and remove allergens or undesired substances.

In medicine, the use of genome editing is commonplace in stem cell research, and the techniques are increasingly used in development work especially regarding gene and genotype research, with which the aim is to increase the understanding and development of gene therapy. Modelling of diseases and development of gene therapy using test animals or cell models, as well as analyses of the connections between disease and cell function are already carried out using genome editing. Targeted genome editing techniques are not yet developed enough to be in common clinical use in the near future. On the longer term, the utilisation of genome editing will not only increase not only in the development of medicine, but also in gene therapy.

In veterinary medicine and animal breeding, the new genome editing techniques are not yet utilised, but the development of the field and opportunities are being examined. Possible applications already identified include, for example, increasing resistance and removing the horns of cattle. This is mainly to increase the well-being of animals. Animal physiology already utilises models produced with genome editing in a way similar to medical science.

The operators emphasise that small companies are significant actors, especially in the development of techniques. In plant breeding, the current view is that at the moment, in practice only large companies have the resources to utilise genome editing due the high costs of the risk analyses necessitated by current regulations. Finnish companies, however, are well prepared to use genome editing techniques, should public attitudes become more permissive.

Companies view the advances made possible and accelerated by genome editing to be dependent on both the development of legislation as well as consumers' attitude towards those advnaces. The private sector clearly wants to be able to better anticipate regulation and increase government cooperation to promote both uptake and opportunities for genome editing research. Moreover, not only companies specifically, but also researchers,call for a new type of risk analysis method related to the use of technologies, which would simultaneously consider the risks and possibilities.

From a global perspective, European and domestic regulation is perceived as conservative and limiting for research, innovation, and business as a whole. Furthermore, consumer attitudes are seen to further limit the research, application, and utilisation of technologies. It is seen that the stubborn beliefs limit demand, despite the end product being safe. The brewing industry and activities based on organic production, for instance, have categorically prohibited the use of genome editing techniques in their operations.

Amongst the actors, the worry related to the international aspect is that the EU will be left behind in research, applications, and innovations, unless changes in regulation and public opinions come to pass. The use of a common regulatory framework in the EU was seen as an essential means to advance both research as well as development and applications. Although there are plenty of ideas for applications based on genome editing, in Europe the actors have not yet dared to use the techniques on a large scale to bring them into being primarily due to the strict regulations and the consumers' stance.

Researchers wish that, instead of new genome editing regulations, the regulatory regime would be focused on end products. This would assist in prevention of unwanted outcomes and unfetter research and product development. However, it is still unclear what legislation should be applied. Researchers have mentioned that new genome editing techniques should be examined by sector, because intended uses vary greatly between sectors.

The public sector has many roles as an actor in the field of genome editing. Legislation, licensing, control, regulation, and funding, amongst others, are the functions of the public sector. Currently, the roles of the varied public sector actors regarding new genome editing techniques and their regulation are considered difficult to understand. Regulatory

guidelines regarding import and use are considered fragmented and ambiguous, especially amongst companies and research actors. This is seen to hamper the research, application, and commercialisation of the technologies. Regarding control, however, Finland is seen to be on a good level. Still, the actors are worried about how the control of new genome editing techniques can be implemented in practice.

Possession and regulation of information are seen to be scattered among different administrative sectors. Actors support the idea of founding a genome centre in which information would be aggregated for development, application, import, and export. The role of the genome centre would be, however, limited, as it has been planned only to be used in the processing of genome information regarding the improvement of human health[91].

Amongst researchers, there are no significant threats identified in the utilisation of new genome editing techniques. The biggest threat would seem to be that of misuse of technologies. Some sort of threat might also be created if gene drives are used to control invasive species, which might lead to changes in the ecosystem. From the perspective of organic production, the danger of mixing organically produced material with material produced with new genome editing techniques constitutes a big threat.

Instead, the accuracy of the new technologies would expedite research and development significantly, which could lead to genome editing having massive economic, social, and environmental effects in the future. The significance of genome editing would be substantial in plant breeding for the adaptation to the challenges of climate change, in breeding to improve animals' well-being, and in the treatment and understanding of diseases in medicine, specifically. Furthermore, in the food industry, the significant opportunities include enabling quicker and cleaner production, especially when combined with synthetic biology, for instance in the production of enzymes.

Based on interviews, experts uniformly seem to be of the opinion that comprehension of new genome editing techniques amongst the general public should be increased. This should be started already during secondary school, not just in connection with university studies. The negative views that consumers have of genome editing techniques is mainly due to lack of knowledge. Average people equate genome editing with genetic modification. Furthermore, even some of the experts think that the use of new genome techniques is the same as genetic modification.

91 https://stm.fi/en/genome-center

As a conclusion, the table below summarizes the insight gained with this survey regarding the possibilities and threats of the new genome editing techniques in the sectors surveyed.

Table 4. A summary of the possibilities and threats of the new genome editing techniques in plant breeding, animal breeding, and medicine.

Sector	Possibilities	Threats
Plant breeding	More accurate and rapid plant breeding with which to respond to challenges created by climate change and population growth as well as to improve the nutritional quality, remove allergens, etc.	Intentional misuse Non-use Organisms created with genome editing get mixed with organic products
Animal breeding	Improving the health and wellbeing of animals Avoiding antimicrobial resistance	An unexpected change (mutation) harmful to an animal
Medicine	Precise medical research Gene therapy	Terrorist use, biological warfare Mental image threat, irresponsible use (altering the human germline)

11 Conclusion

In conclusion, the new genome editing techniques are seen to have great potential for plant breeding, animal breeding, and medicine regarding both useful applications and economic growth. Currently in Finland, genome editing activities are being used in basic research in plant biology and in plant breeding. Animal physiology in Finland utilises model organisms created with new genome editing techniques. These are complemented by their development for animal and cell models and for gene therapy methods in medicine, especially focusing on rare hereditary diseases. In animal and plant breeding programs, genome editing techniques are not yet being utilised.

It is unlikely that there will be a transition from the use of new genome editing techniques in research to the development of products before the legislative issues are clarified and products created using new genome editing techniques are exempted from regulation as GMOs. Another factor hindering the use of genome editing for products in the European market is the overall unwelcoming stance of the public towards genetic engineering. Therefore, more dialogue is needed between researchers, government, and the public. For the dialogue to be possible, a basic understanding of genome editing should be conveyed in secondary school, not only at university. This would help citizens form knowledge-based view of genome editing.

The outcome of this report can be summarised in the words of one of the interviewed researchers:

> ***'that Europe will become a museum of research and development if GE cannot be applied in the EU. The innovations and new products will happen elsewhere.'***
> [research representative]

Appendices

APPENDIX 1: Interview frame

Utilisation of New Genome Editing Techniques in Finland

Interview, date:

Interviewee, position, and location:

Sector: basic research, agricultural, biotechnology, medicine, and environmental sectors

Project introduction
Utilisation of New Genome Editing Techniques in Finland

Government's analysis, assessment, and research activities VN-TEAS 7.9 Utilisation of New Genome editing techniques in Finland

Consortium
VTT, Demos Helsinki and LUKE

Timetable
Autumn 2020 – Spring 2021

Additional information: Senior Scientist Nina Wessberg, VTT, nina.wessberg@vtt.fi, tel. +358 (0) 40 742 8185

Consent:
Can the interview be recorded for research purposes (transcription, analysis)? repetition in the recording

Subproject 1: CURRENT STATE

- To what extent are you currently using new genome editing techniques?
- For what purposes are you using the new techniques at the moment?
- What future uses can you identify?

- If you do not use them, do you know how others in your field are using them?
- Do you or your sector have abilities and resources to use the techniques in question yourself? If not, what kind of obstacles are there?
- What is your opinion on how the education system supports the use of new genome editing techniques?
- Do you see a need for reform in the education? To whom should education be targeted especially?

Subproject 2: INTERNATIONAL SCOPE

- Is the possible use/need for the use based on import in your sector? If yes:

    - What kind of applications is it about? Is it about organisms edited with new genome editing techniques or products created using them?
    - What are/would be the probable countries of origin?
    - What is/would be the possible volume of import?

- Does your sector have the need to import organisms edited with new genome editing techniques, products produced using them or innovations related to the techniques? If yes, where would the exports be directed to?
- What kind of international cooperation is the use related to in your operations and/or sector?

Subproject 3: THE FUTURE, THREATS AND POSSIBILITIES

- In what direction does your operation/sector anticipate the new genome editing techniques will develop for example within the coming 10 years here and elsewhere?
- How would you evaluate the economic significance of genome editing techniques?
- In your opinion, what kind of realistic biothreats are related to the different application of new genome editing techniques in your sector?
- Which of them should the authorities specifically prepare for?
- Is the use/non-use of the techniques related to national preparations for other types of threats (for instance, climate change and food security)?

Depending on sector, ask:

- How are the new genome editing techniques related to public health (medicine, vaccines, gene therapy products or the health effects of food)?

Can you suggest any other people we could interview?

APPENDIX 2: The Programme of the Opening Meeting

Virtual Breakfast with the Genome Project

June 16, 2020 at 9:00–11:00
Zoom Workshop
https://zoom.us/j/99207814713?pwd=dkEvZlVMU09ITVNubnVnbUFIMjhIQT09

8:45 Opening Zoom for Testing the Connection

9:00 Welcome & Opening the Event
Nina Wessberg, VTT
Chris Rowley & Liisa Kolehmainen, Demos Helsinki

9:10 Administration's Speech
Kirsi Törmäkangas, STM

9:20 Presenting the Research Plan
Nina Wessberg, VTT

9:35 Overview of the Current Situation
Johanna Vilkki, LUKE

9:45 Group discussion 1: Need for Use and Regulation
In theme groups:

- What do you think of the research plan?
- For what purposes are/could the genome editing techniques be used?
- What is your current view on the regulation of the techniques?
- What kind of legislation would enable the desired use?

10:25 Group discussion 2: Attitudes and Business
In mixed groups:

- What is your experience regarding the attitudes towards genome editing techniques?
- What kind of business potential do you see in the use of the techniques?
- How should the consumers and patients be informed about and involved in the use of the techniques in consumer products and treatments?

10:50 Final Conversation & Greetings to the Research Group

11:00 Thanks & Ending the Event

APPENDIX 3: The Programme of the Stakeholder Workshop

Utilisation of New Genome Editing Techniques in Finland: Development and Opportunities Across Industries

Zoom workshop December 9, 2020

9:00 Opening the Event Satu Korhonen, Demos Helsinki

9:05 New Genome Editing Techniques in Finland – Results of the Report
Nina Wessberg, VTT
Satu Korhonen, Demos Helsinki

10:00 Brightening the Possibilities and Challenges of the Future from Different
Perspectives:

- Business
- Daily life
- Society

11:20 Summary of the Results of the Workshop and the Next Steps

11:30 Workshop ends

SOURCES AND FURTHER READING

Agustina I. Whelan, Patricia Gutti and Martin A. Lema. Gene Editing Regulation and Innovation Economics. Front. Bioeng. Biotechnol., 15 April 2020 | https://doi.org/10.3389/fbioe.2020.00303

Ahteensuu, M., Grönholm, M., Joutsjoki, V., Jäntti, J., Lohtander-Buckbee, K., Ritala-Nurmi, A., ... Teeri, T. (2018). *Geenien muokkaus uusilla tekniikoilla - kasvit, eläimet, mikrobit*. (BTNK:n julkaisu; No. 8). Helsinki: Biotekniikan neuvottelukunta.

Alavuotunki, A., Koivisto, R., Kauppinen, V., Törmäkangas, K., & Wessberg, N. (2002). Prosessiteollisuuden käytännöistä hyötyä geenitekniikalla muunnettujen kasvien riskinarvioinnissa. Kemia-Kemi, 29(2), 35-37.

Alexandratos N, Bruinsma J. World agriculture towards 2030/2050: the 2012 revision. 2030. http://www.fao.org/fileadmin/templates/esa/Global_persepctives/world_ag_2030_50_2012_rev.pdf

ALLEA (2020) lead authors: Dima, O.; Bocken H.; Custers, R.; Inze, D.; Puigdomenech, P.; Genome Editing for Crop Improvement. Symposium summary. Berlin. DOI: 10.26356/gen-editing-crop

Anna Wilkinson. Genome editing to improve farmed animal welfare. What's not to like? 19 Feb 2020. Nuffield Council on Bioethics. https://www.nuffieldbioethics.org/blog/genome-editing-to-improve-farmed-animal-welfare-whats-not-to-like

Araki, M. & Ishii, T. 2015. Towards social acceptance of plant breeding by genome editing. *Trends in Plant Science, 20*(3), pp. 145-149. doi:10.1016/j.tplants.2015.01.010

Ashley Taylor. Gene Editing Meets The Food Supply - The New World of Custom-Designed Crops. July 29, 2019. Milken Institute Review. https://www.milkenreview.org/articles/gene-editing-meets-the-food-supply

Bayer, BASF to pursue plant gene editing elsewhere after EU ruling. Reuters. July 27, 2018. https://www.reuters.com/article/us-eu-court-gmo-companies-idUSKBN1KH1NF

Bellini J. This gene-edited calf could transform Brazil's beef industry. https://www.wsj.com/video/series/moving-upstream/this-gene-edited-calf-could-transform-brazil-beef-industry/D2D93B49-8251-405F-BC35-1E5C33FA08AF

Biotekniikan neuvottelukunta, Geenien muokkaus uusilla tekniikoilla, 2018, Helsinki.

Brinegar, K., K. Yetisen, A., Choi, S., Vallillo, E., Ruiz-Esparza, G. U., Prabhakar, A. M., . . . Yun, S. 2017. The commercialization of genome-editing technologies. *Critical Reviews in Biotechnology, 37*(7), pp. 924-932. doi:10.1080/07388551.2016.1271768

Bruce, A. Genome edited animals: Learning from GM crops? *Transgenic Res* 26, 385–398 (2017). https://doi.org/10.1007/s11248-017-0017-2

Bruce, A., Bruce, D. Genome Editing and Responsible Innovation, Can They Be Reconciled?. *J Agric Environ Ethics* 32, 769–788 (2019). https://doi.org/10.1007/s10806-019-09789-w

Callaway, Ewen. CRISPR plants now subject to tough GM laws in European Union. Nature 560, 16 (2018) doi: https://doi.org/10.1038/d41586-018-05814-6

Cavaliere, Giulia (2019). WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing, Background Paper: The Ethics of Human Genome Editing. https://www.who.int/ethics/topics/human-genome-editing/WHO-Commissioned-Ethics-paper-March19.pdf

Celine-Lea Halioua-Haubold, James G. Peyer, James A. Smith, Zeeshaan Arshad, Matthew Scholz, David A. Brindley and Robert E. MacLareng. Regulatory Considerations for Gene Therapy Products in the US, EU, and Japan. Yale J Biol Med. 2017 Dec; 90(4): 683–693. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5733859/

Chris Proudfoot, Simon Lillico, Christine Tait-Burkard, Genome editing for disease resistance in pigs and chickens, Animal Frontiers, Volume 9, Issue 3, July 2019, Pages 6–12, https://doi.org/10.1093/af/vfz013

Dennis Eriksson, Drew Kershen, Alexandre Nepomuceno, Barry J. Pogson, Humberto Prieto, Kai Purnhagen, Stuart Smyth, Justus Wesseler, Agustina Whelan. 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 (2019) 222: 1673–1684. https://doi.org/10.1111/nph.15627

E. Woźniak, A. Tyczewska, and T. Twardowski. A Shift Towards Biotechnology: Social Opinion in the EU. Trends in Biotechnology, March 2021, Vol. 39, No. 3 DOI: https://doi.org/10.1016/j.tibtech.2020.08.001

Ellens, K.W., Levac, D., Pearson, C. *et al.* Canadian regulatory aspects of gene editing technologies. *Transgenic Res* 28, 165–168 (2019). https://doi.org/10.1007/s11248-019-00153-2

Eriksson, D. The evolving EU regulatory framework for precision breeding. Theor Appl Genet 132, 569–573 (2019). https://doi.org/10.1007/s00122-018-3200-9

Geeniteknologia. Helsinki, Tulevaisuusvaliokunta, 2018. 37 s. Eduskunnan tulevaisuusvaliokunnan julkaisu 2/2018.

Habets, M., Hove, L. van and R. van Est (2019). Genome editing in plants and crops – Towards a modern biotechnology policy focused on differences in risks and broader considerations. The Hague: Rathenau Instituut

Huson Hj, Kim ES Godfrey RW, et al. 2014.Genome-wide association study and ancestral origins of the slick-hair coat in tropically adapted cattle. Frontiers in genetics 5:101

James R. Clapper, Director of National Intelligence. Statement for the Record, Worldwide Threat Assessment of the US Intelligence Community, Senate Armed Services Committee. February 9, 2016. https://www.dni.gov/files/documents/SASC_Unclassified_2016_ATA_SFR_FINAL.pdf

Jasanoff, Sheila (2016). The ethics of invention: technology and the human future. W.W. Norton & Company, New York 2016.

Jochen Menz, Dominik Modrzejewski, Frank Hartung, Ralf Wilhelm and Thorben Sprink. Genome Edited Crops Touch the Market: A View on the Global Development and Regulatory Environment. Front. Plant Sci., 09 October 2020 | https://doi.org/10.3389/fpls.2020.586027

Jokela, M., Oja-Leikas, M. & Rova, M. (eds.). *Kiehtovat geenit : mihin geenitietoa käytetään?.* 1. p. ed. Helsinki: Duodecim

Jorasch P (2020) Potential, Challenges, and Threats for the Application of New Breeding Techniques by the Private Plant Breeding Sector in the EU. Front. Plant Sci. 11:582011. doi: 10.3389/fpls.2020.582011

Linturi, Risto: Geeniteknologian kehitys 2018–2020 eri merkitysaloilla. Helsinki, Tulevaisuusvaliokunta, 2020. 25 s. Eduskunnan tulevaisuusvaliokunnan julkaisu 2/2020.

Malyska, A., Bolla, R. & Twardowski, T. 2016. The Role of Public Opinion in Shaping Trajectories of Agricultural Biotechnology. *Trends in Biotechnology, 34*(7), pp. 530-534. doi:10.1016/j.tibtech.2016.03.005

Martin Wasmer. Roads Forward for European GMO Policy – Uncertainties in Wake of ECJ Judgment Have to be Mitigated by Regulatory Reform. Front Bioeng Biotechnol. 2019; 7: 132. Published online 2019 Jun 5. doi: 10.3389/fbioe.2019.00132

Matthew P. Hirakawa, Raga Krishnakumar, Jerilyn A. Timlin, James P. Carney, Kimberly S. Butler; Gene editing and CRISPR in the clinic: current and future perspectives. *Biosci Rep* 30 April 2020; 40 (4): BSR20200127. doi: https://doi.org/10.1042/BSR20200127

Max Planck Society. Discussion paper focusing on the scientific relevance of genome editing and on the ethical, legal and societal issues potentially involved (2017). https://www.mpg.de/13811476/DP-Genome-Editing-EN-Web.pdf

Maywa Montenegro de Wit; Democratizing CRISPR? Stories, practices, and politics of science and governance on the agricultural gene editing frontier. *Elementa: Science of the Anthropocene* 1 January 2020; 8 9. doi: https://doi.org/10.1525/elementa.405

Mukherjee, Siddharta (2019). Geeni - Intiimi historia. Vastapaino Tampere.

Modrzejewski, D., Hartung, F., Sprink, T. *et al*. 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 (2019). https://doi.org/10.1186/s13750-019-0171-5

Myhr A.I., Grønsberg I.M., Okoli A.S. (2020) Norway—The Norwegian Gene Technology Act: Presenting Case Studies to Illustate the Act's Advances in Protecting Biodiversity. In: Chaurasia A., Hawksworth D.L., Pessoa de Miranda M. (eds) GMOs. Topics in Biodiversity and Conservation, vol 19. Springer, Cham. https://doi.org/10.1007/978-3-030-53183-6_41

Niiler, E . 2018. How Crispr could transform our food supply. National Geographic, August 10. https://www.nationalgeographic.com/environment/future-of-food/food-technology-gene-editing/

Nuffield Council on Bioethics. Genome editing: An ethical review (2016). http://nuffieldbioethics.org/project/genome-editing/ethical-reviewpublished-september-2016

Pursel VG, Hammer RE, Bolt DJ, Palmiter RD, Brinster RL. Integration, expression and germ-line transmission of growth-related genes in pigs. J Reprod Fertil Suppl. 1990;41:77-87. PMID: 2213718.

Raimo Lahti (toim.). Biolääketiede, tutkimus ja oikeus / Helsingin yliopiston oikeustieteellinen tiedekunta, 2012.

Richard Gray, "Why gene editing could create so many jobs". BBC. 15th October 2018. https://www.bbc.com/worklife/article/20181003-why-gene-therapy-will-create-so-many-jobs

Sarah M Schmidt, Melinda Belisle, Wolf B Frommer. The evolving landscape around genome editing in agriculture. EMBO Rep (2020)21:e50680https://doi.org/10.15252/embr.202050680

Sarewitz, Daniel. CRISPR: Science can't solve it. 23 June 2015 Nature 522, 413–414 (25 June 2015) doi:10.1038/522413a

Schulman, A.H., Oksman-Caldentey, K.-M. & Teeri, T.H. (2020). European Court of Justice delivers no justice to Europe on genome-edited crops. Plant Biotechnology Journal 18: 8-10. https://doi.org/10.1111/pbi.13200

Sini Tervo. 2018. Perimään puuttumisen juridiset ulottuvuudet perinnöllisten sairauksien hoidossa /Pro gradu -tutkielma.

Sirpa Soini. Biopankkitoiminnan haasteet jälkigenomisella ajalla: onko biopankkilakiesitys ajantasalla? / Julkaisussa: Biolääketiede, tutkimus ja oikeus / Raimo Lahti (toim.). s. 223–246.

Sumant Ugalmugle, Rupali Swain, "Gene Editing Market worth over $10bn by 2026". Global Market Insights. October 1, 2020. https://www.gminsights.com/pressrelease/gene-editing-market

Tait-Burkard, C., Doeschl-Wilson, A., McGrew, M.J. *et al.* Livestock 2.0 – genome editing for fitter, healthier, and more productive farmed animals. *Genome Biol* 19, 204 (2018). https://doi.org/10.1186/s13059-018-1583-1

Tervo, Sini (2018). Perimään puuttumisen juridiset ulottuvuudet perinnöllisten sairauksien hoidossa /Pro gradu -tutkielma. Helsingin yliopisto, Oikeustieteellinen tiedekunta, 2018.

Tetsuya Ishii & Motoko Araki (2017) A future scenario of the global regulatory landscape regarding genome-edited crops, GM Crops & Food, 8:1, 44-56, DOI: 10.1080/21645698.2016.1261787

The Norwegian Biotechnology Advisory Board (Bioteknologirådet). Norwegian consumers' attitudes toward gene editing in Norwegian agriculture and aquaculture. 2 April 2020. https://www.bioteknologiradet.no/filarkiv/2020/04/Report-consumer-attitudes-to-gene-editing-agri-and-aqua-FINAL.pdf

The Norwegian Biotechnology Advisory Board (Bioteknologirådet). The Gene Technology Act – Invitation to Public Debate. 2018. https://www.bioteknologiradet.no/filarkiv/2010/07/genteknologiloven-engelsk-hele-for-web-v-2.pdf

Ulrica Gabrielsson, Anneli Törrönen. Genomitieto kertoo : mistä tulemme, mihin menemme. ; Tutkijoiden ja kansanedustajien seura Tutkas 2012.

Van der Meer, P., Angenon, G., Bergmans H., Buhk, H., Callebaut, S., Chamon, M., Zimny, T. (2021). The Status under EU Law of Organisms Developed through Novel Genomic Techniques. *European Journal of Risk Regulation,* 1-20. doi:10.1017/err.2020.105

Wartiovaara, Kirmo: Tulevaisuuden solu- ja geenihoitojen mahdollisuudet, 137-138. Robotiikka, geenitekniikka, etiikka. Toimittanut Esa Erävalo. Ajatushautomo Kompassi ry, 2017.

VNK 2020. Innovaatiomyönteinen sääntely: Nykytila ja hyvät käytännöt. Valtioneuvoston selvitys- ja tutkimustoiminnan julkaisusarja 2020:27

Young AE, Mansour TA McNabb BR, Owen JR, Trott JF, Brown CT, Van Eenennaam AL.2019. Genomic and phenotypic analyses of six offspring of a genome-edited horn-less bull. Nature Biotechnology

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