Genome Editing and Engineering
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Module - 12
Ethical concerns: Germ line gene editing
Lecture - 49
Regulatory issues in Genome Editing

Welcome to my course on Genome Editing and Engineering. We are discussing module 12 and in this lecture number 2 we will be discussing about the Regulatory issues in Genome editing. We have discussed about the various ethical concerns. So, there is a need for regulation to take care of many of those critical issues.

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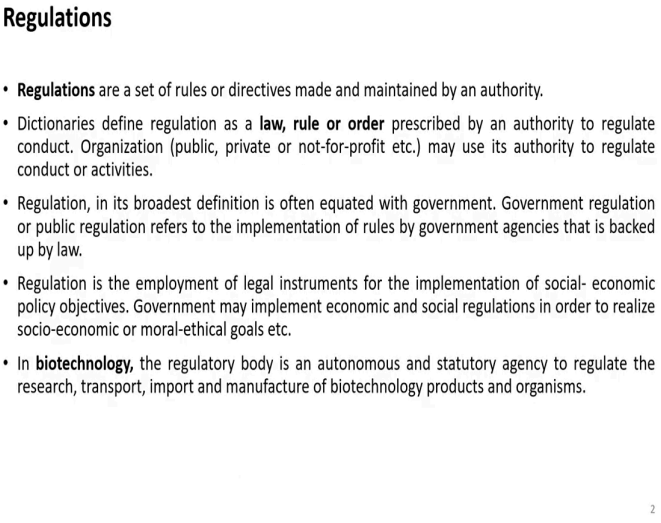

What do we mean by regulations? In general, regulations are a set of rules or directives made and maintained by an authority. Dictionary meaning of regulation is presented as a law, rule or order prescribed by an authority to regulate conduct. Organizations may use its authority to regulate or conduct the activities.

Regulation, in its broadest definition is often equated with government. Government regulation or public regulation refers to the implementation of rules by government agencies that is backed up by legal instruments.

Regulation is basically the employment of the legal instruments for the implementation of social-economic policy objectives. Common may implement economic and social regulations in order to realize socio-economic or moral-ethical goals etcetera.

In biotechnology, the regulatory body is an autonomous and statutory agency to regulate the research, transport, import and manufacture of biotechnology products and organisms.

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From the mid and late 1970s and through the 1980s and 90s, new biotechnology development has been a subject of debate and regulation is most in most industrialized nations.

Environmental, health, societal and ethical consequences have been on the political agenda nationally and internationally, with debates being triggered by the first successful gene transfers in 73 and 74.

However, too much regulation beyond the requirement may play spoilsport such as the assumed negative impacts of regulation on innovation and economic growth in economies of innovation and in industrial policy; the inhibiting consequences of public debate and critic assumed by industrial strategies.

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So, this is a picture obtained from the website of Gordon Research Conference, these conference being listed as a conference on nucleic acids held in June, 1973. It was a public event where discussions regarding the safety and risks of rDNA research was initiated.

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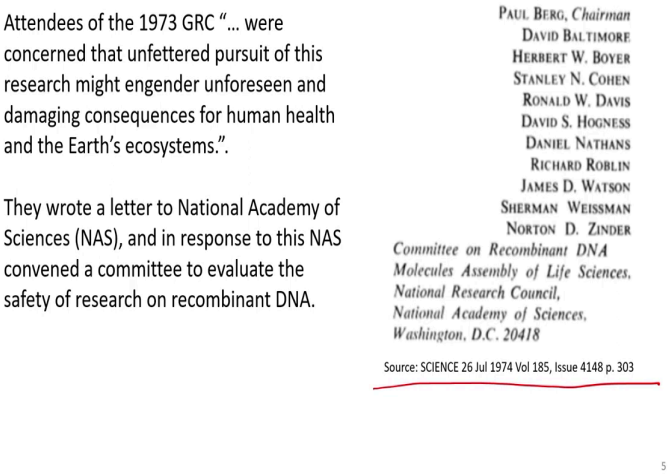

Attendees of these conference mostly scientists were concerned that unfettered pursuit of this research might engender unforeseen and damaging consequences for human health and the Earth's ecosystem. They wrote a letter to National Academy of Sciences United States and in

response to these NAS convened a committee to evaluate the safety of research of a recombinant DNA.

And, the members of these committee as obtained from the journal SCIENCE 26 article is Paul Bero one of the pioneers of the recombinant DNA technology. David Baltimore, Herbert Boyer, Stanley Cohen, Ronald Davis, David Hogness, Daniel Nathans, Richard Roblin, James D Watson, Sherman Weissman, Norton D Zinder. So, this is the committee on recombinant DNA Molecules Assembly of Life Sciences, National Research Council, National Academy of Sciences, Washington D. C.

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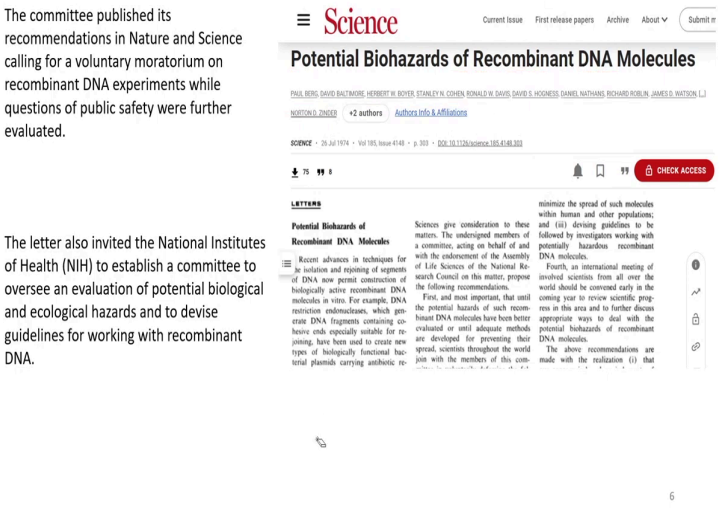

The committee published its recommendations in two journals namely Nature and Science in 1974 and calling for a voluntary moratorium on recombinant DNA experiments while questions of public safety were further evaluated. And, the name of these article in the science is the Potential Biohazards of Recombinant DNA Molecules and you can see in the authors list the name of the committee members constituted by NAS.

In this letter, they invited the National Institutes of Health to establish a committee to oversee an evolution of potential biological and ecological hazards and to devise guidelines for working with recombinant DNA.

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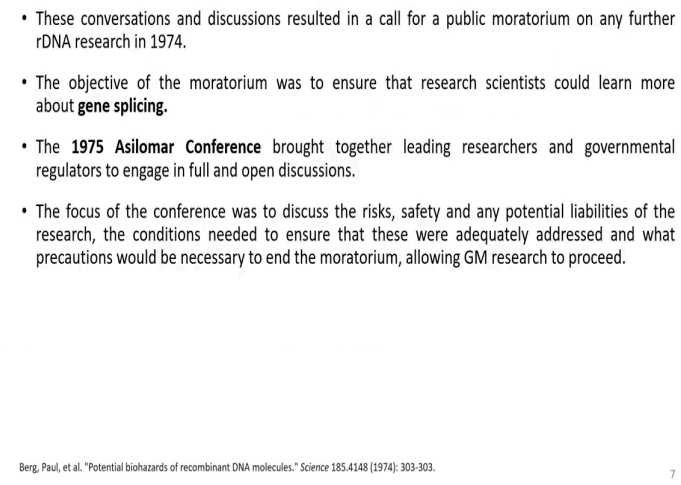

These are many conversations and discussions resulting in a call for a public moratorium on any further rDNA research. The objective of the moratorium was to ensure that research scientists could learn more about gene splicing, editing and gene transfer.

The 1975 Asilomar Conference about which we have discussed in the last lecture brought together leading researches and governmental regulators to engage in full and open discussions.

The focus of these Asilomar conference was to discuss the risks safety and any potential liabilities of the research about which you are already aware, the conditions needed to ensure that these were adequately addressed and what precautions could would be necessary to end the moratorium, allowing genetic modification research to proceed.

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With the world's leading rDNA recombinant DNA research experts in presence, the Asilomar Conference was able to develop safe research guidelines and practices themselves, rather than having them imposed by government agencies. The participation officials of the US National Institute of Health enhanced the transparency for scientific and public scrutiny however.

Appropriate steps were taken to ensure the province of any risks regarding containment standards for virus and bacteria research that could potentially harm humans if widespread exposure occurred. Knowledge about the application of recombinant DNA research grew rapidly moving from the initial bacterial research in the mid 70s to plants in the early 1980s.

In 83, the Miami Winter Symposium on the molecular genetics of plant was held and was sharing of knowledge about applying gene technology to agriculture which no discussions about the potential rigs of GM plants or about how to regulate the technology.

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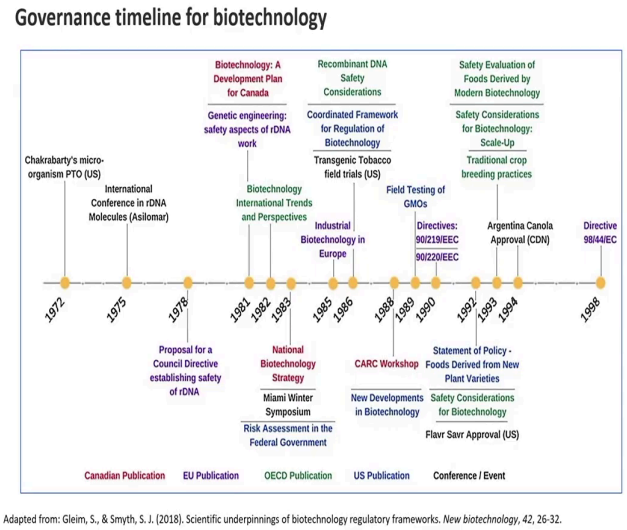

Adapted from: Gleim, S., & Smyth, S. J. (2018). Scientific underpinnings of biotechnology regulatory frameworks. *New biotechnology*, *42*, 26-32. 9

So, this is a brief timeline on the governance on or for biotechnology you can see in 1972 the first patent on a live organisms was awarded to Chakrabarty, and then in 1975 the international conference in rDNA recombinant DNA molecules was held prior to that the Gordon research conference was held as we have already just discussed.

And, then by 78 there was a proposal for a council directive establishing safety of recombinant DNA and in the years 81 to 83, there were many activities. In 81, Biotechnology: A development plan for Canada; Genetic engineering safety: aspect of rDNA work was established; Biotechnology International Trends and Perspectives in 82. Then, in 83 the National Biotechnology Strategy; Miami Winter Symposium, here the risk assessment in the Federal Government was developed. Then 85, we can see the development of industrial biotechnology in Europe and 86 the Recombinant DNA Safety Considerations coordinated framework for Regulation of Biotechnology and Transonic tobacco field trails in the US took place.

After 2 years in 88, there was a CARC workshop New Developments in Biotechnology and Field Testing of GMOs occurred in 89. Then there are several directives issued in 1990. 92 hundred 19 EEC and 92 20 EEC and in 1992 Statement of Policy Foods Derived from New Plant Varieties and Safety Considerations for Biotechnology were coming up and the Flavr Savr Tomato was approved in the USA.

In 1993, there was the Safety Evaluation of Foods derived by Modern Biotechnology and Safety Considerations of Biotechnology Scale-up and traditional crop breeding practices. And, the Argentinian Canola case came up and there was a approval in the CDN in 1994 and in 1998 the Directive number 98 oblique 44 by EC was issued.

So, this is in brief about the various events that occurred regarding the governance of timeline for biotechnology.

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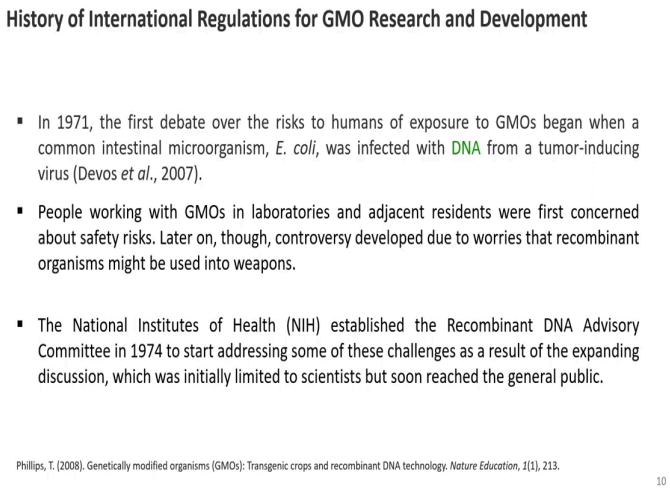

Let us now look into the brief history of international regulations of genetically modified organism research and development. In 1971, the first debate about over the risks of humans to exposure of genetically modified organisms began when a common intestinal microorganism, E. coli, was infected with DNA from a tumor-inducing virus.

People working with GMOs in laboratories and adjacent residents were first concerned about safety risks. Later on, through controversy though, controversy developed due to worries that recombinant organisms might be used into biological weapons.

The National Institutes of Health established the Recombinant DNA Advisory Committee in 1974 to start addressing some of these challenges as a result of the expanding discussion, which was initially limited to scientists, but soon reached the general public.

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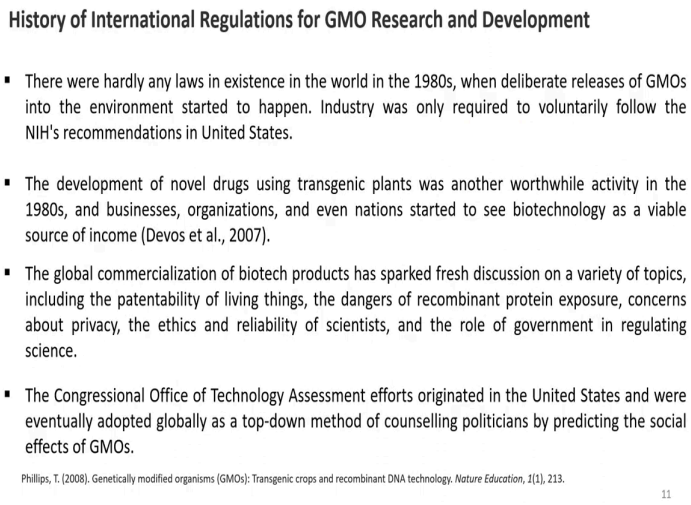

In the 1980s, there were hardly any laws existing in US or even the world when delivered release of genetically modified organisms into the environment started to happen. Industry was only required to voluntarily follow the NIHS recommendations in the United States.

The development of novel drugs using transonic plants was another worldwide activity in the 80s, and businesses, organizations, and even nations started to see biotechnology as a viable source of income. The global commercialization of biotech products has sparked fresh discussions on a variety of topics including the patentability of living organisms, the dangers of recombinant protein exposure, concerns about privacy, the ethics and reliability of scientists, and the role of government in regulating science.

The Congressional Office of Technology Assessment efforts originated in the United States and were eventually adopted globally as a top-down method of counseling politicians by predicting the social effects of genetically modified organisms.

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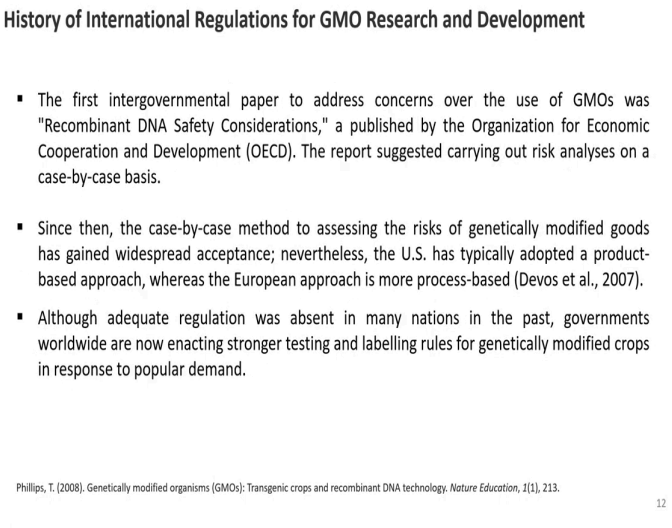

The first intergovernmental paper to address concerns over the use of GMOs was Recombinant DNA Safety Considerations, a published by the Organization for Economic Cooperation and Development. The report suggested carrying out risks analysis on a case-by-case basis.

Since then, the case-by-case method to assess the risks of genetically modified goods has gained widespread acceptance, and nevertheless, the US has typically adopted the product-based approach, whereas, the European approach is more process-based.

Although adequate regulation was absent in many nations in the past, governments worldwide are now enacting stronger testing and levelling rules for genetically modified crops in response to public popular demand.

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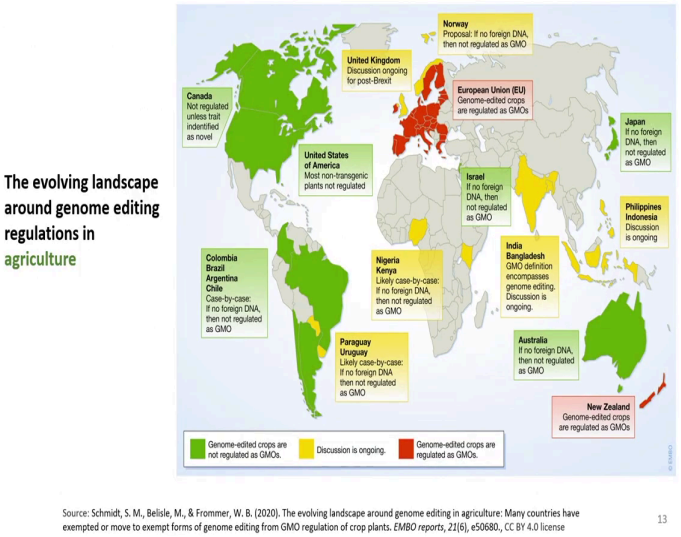

This is a evolving landscape around genome editing regulations in agriculture. So, you can see the green countries are the ones where genome edited crops are not regulated as genetically modified organisms. As for example, Canada, then Colombia, Brazil, Argentina and Chile where case-by-case if no foreign DNA, then not regulated as GMO.

So, in gene editing we may simply edit or delete portions of a gene or we may change the base of a particular protein or a particular gene sequence. So, they do not qualify to be considered as GMO as parties definition in the Latin American countries.

In Canada regulation is not there unless trait is identified as novel and in the United States of America most non-transonic plants are not regulated. There are other countries which are shown by the yellow color where discussions are going on which include India and Bangladesh. The GMO definition encompasses genome editing in this case in India and discussion is was going on at the time of the publication of these map in 2020 in this particular journal.

However, they are a block of countries in Europe which you can see are totally marked in red where genome edited crops are regulated as genetically modified organisms. So, this is a landscape overall regarding the regulation of genome editing in agriculture across the globe.

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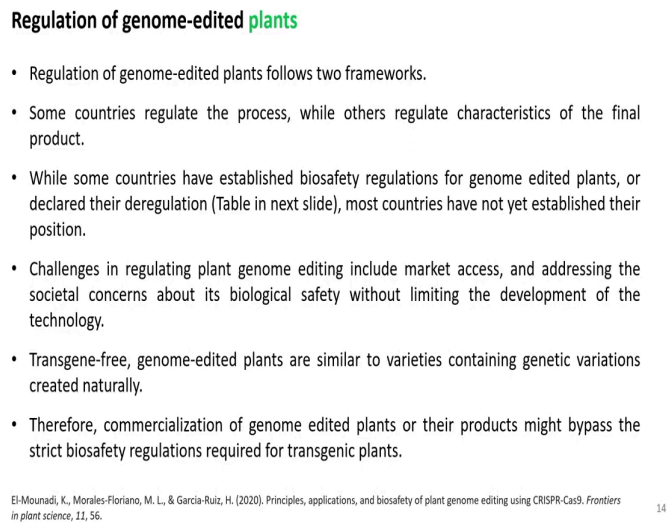

Regulation of genome edited plants follow two frameworks. Some countries regulate the process, while others regulate characteristics of the final product. While some countries have established bio safety regulations for genome edited plants, or declared deregulation, most countries have not yet established their position.

Challenges in regulating plant genome editing includes market access and addressing the societal concerns about it is biological safety without limiting development of the technology transgene-free, genome-edited plants are similar to varieties containing genetic variations created naturally.

Therefore, commercialization of genomic edited plants or their products might bypass the strict biosafety regulations required for transgenic plants.

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Regulation of genetically modified and genome edited **plants** across countries.

Country	Genetically modified plants[1]	Genome-edited plants[2]
Argentina	Regulated	Case-by-case, mostly non-regulated
Australia	Regulated	Non-regulated
Brazil	Regulated	Case-by-case, mostly non-regulated
Canada	Regulated	Regulated
Chile	Regulated	Case-by-case, mostly non-regulated
European Union	Regulated/opposed	Regulated/Opposed
India	Regulated	Regulated
Japan	Regulated	Non-regulated
Malaysia	Regulated	Regulated
Mexico	Regulated	Regulated
New Zealand	Regulated	Regulated
South Africa	Regulated	Regulated
Thailand	Regulated	Regulated
United States of America	Regulated	Non-regulated

[1]*Refers to the final product containing transgenes, such as selection markers or other form of foreign DNA used during the process.*
[2]*Refers to the final product lacking transgenes that might have been used during the process.*

El-Mounadi, K., Morales-Floriano, M. L., & Garcia-Ruiz, H. (2020). Principles, applications, and biosafety of plant genome editing using CRISPR-Cas9. *Frontiers in plant science*, *11*, 56.

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So, this table list a regulation of genetically modified and genome edited plants across the globe and you can see the country which are having these genetically modified plants Argentina, Australia, Brazil, Canada, Chile, European Union, India, Japan, Malaysia, Mexico, New Zealand, South Africa Thailand, United States of America and their positioning is different in certain cases it is a case-by-case basis and mostly non-regulated.

And, in many other cases it is regulated or opposed; for example, in the European countries.

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- The United States Department of Agriculture (USDA) declared in March 2018 that genome editing is the **equivalent of conventional breeding** in some instances and therefore **does not require regulatory oversight** within the American regulatory framework.
- A mushroom engineered to resist browning and a **waxy corn** engineered to contain starch composed exclusively of **amylopectin** are the **first CRISPR edited crops** to be approved for commercialization in the USA with **no regulations.**
- The decision not to regulate was based on the fact that no foreign DNA (transgene) was inserted during editing and that the resulting change did not involve resistance to pesticides or herbicides.

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The United States Department of Agriculture declared in March 2018 that genome editing is the equivalent of conventional breeding in some instances and therefore, does not require regulatory oversights within the American regulatory framework. A mushroom engineered to resist browning and a waxy corn engineered to contain starch composed exclusively of amylopectin are the first CRISPR edited crops to be approved for commercialization in the USA with no regulations.

The decision not to regulate was based on the fact that no foreign DNA was inserted during editing and that the result which was obtained did not involve resistance to pesticides or herbicides.

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Regulations in different countries

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Let us now discuss a little bit in detail about the existing regulations or the development of these regulations in different countries across the globe.

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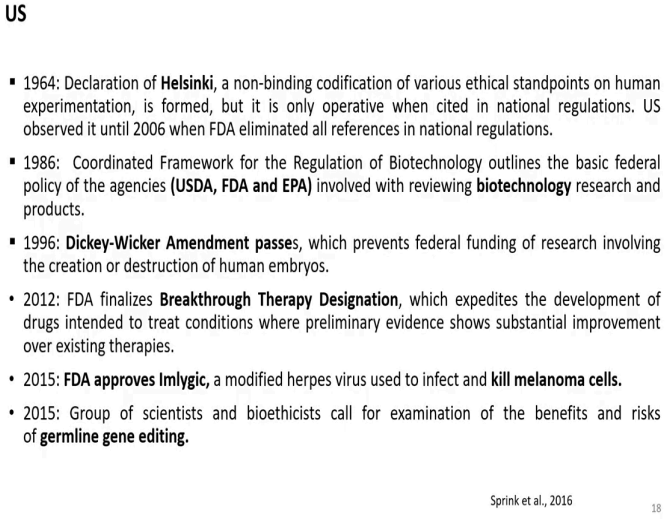

In US in 1964, declaration of Helsinki, a non-binding codification of various ethical standpoints on human experimentation was issued, but it is only operative when cited in national regulations. US observed it until 2006 when FDA eliminated all references in the national regulations.

In 1986, coordinated framework for the Regulation of Biotechnology outlines the basic federal policy of the agencies involved with reviewing biotechnology research and products. In 1996 the Dickey-Wicker amendment passes, which prevents federal funding for research involving the creation or destruction of human embryos.

In 2012 FDA finalizes Breakthrough Therapy Designation, which expedients the development of drugs intended to treat conditions where preliminary evidence shows substantial improvement over existing therapies. In 2015 FDA approves Imlygic, a modified herpes virus used to infect and kill melanoma cells.

In the same year group of scientists and bioethicists calls for examination of the benefits and risks of germline gene editing.

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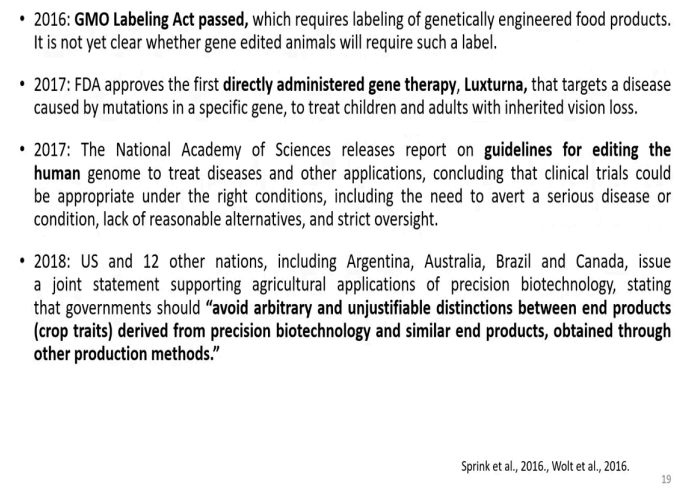

In 2016 GMO Labeling Act was Passed, which required labeling of genetically engineered food products. It is however, not yet clear whether gene edited animas would require such a label. In 2017, FDA approved the first directly administered gene therapy, Luxturna, that targets a disease caused by mutations in a specific gene to treat children and adults with inherited vision loss.

In 2017, the same year The National Academy of Sciences releases report on guidelines for editing the human genome to treat diseases and other applications, in that report concluded that clinical trials could be appropriate under the right conditions, including the need to effort a serious disease or conditions a lack of reasonable alternatives and strict oversight.

In 2018, US and 12 other nations, including Argentina, Australia, Brazil and Canada issued a joint statement supporting agricultural applications of precision biotechnology, stating that government should avoid arbitrary and unjustifiable distinctions between end products derived from precision biotechnology and similar end products, obtained through other production methods.

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In 2019, there were three important developments the first one is that USDA-APHIS proposes new biotechnology framework, a movement of certain genetically engineered organisms also called the SECURE Biotechnology Regulations, which reduces the regulatory requirements for organisms that are unlikely to pause risks to other plants.

The second one is over 300 scientists signed a petition calling for the Harmonization of US gene-edited food regulations, asking the gene editing regulations for animals with the same as for crops and food. The third one is the patients advocacy and the launch by scientist to push a lift on the ban on mitochondrial replacement therapy popularly known as the three-parent IVF with recommendations to loosen restrictions on some form of human germline therapy.

In 2020, FDA releases guidances on gene therapy product development that encourage the development and approval of multiple treatment to create competitive drug markets and provide recommendations to help ensure new products meet the FDA's standard for safety and effectiveness.

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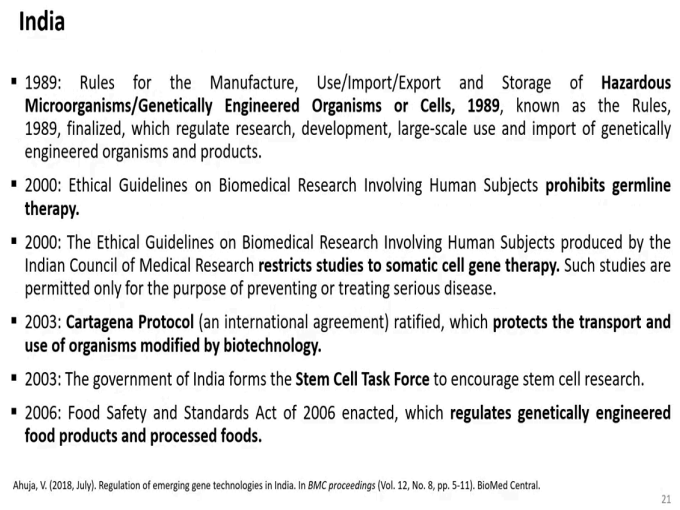

If you look into the regulatory developments in India, in 1989 the rules for the manufacture, use, import, export and stories of hazardous microorganisms or genetically engineered microorganisms or cells, known as the rules 1989, were finalized, which regulate research, development, large-scale use and import of genetically engineered organisms and products.

In 2000, Ethical Guidelines on Biomedical Research Involving Human Subjects was issued which prohibits germline therapy. The same year the ethical guidelines on these biomedical research involving human subjects produced by the ICMR restricted studies on somatic cell gene therapy. Such studies are permitted only for the purpose of preventing or treating serious diseases.

In 2003, Cartagena Protocol was rectified which protects the transport and use of organisms modified by biotechnology and the same year the Government of India formed a stem cell taskforce to encourage stem cell research. In 2006, Food Safety and Standards Act of 2006 was enacted, which regulates genetically engineered food products and processed food.

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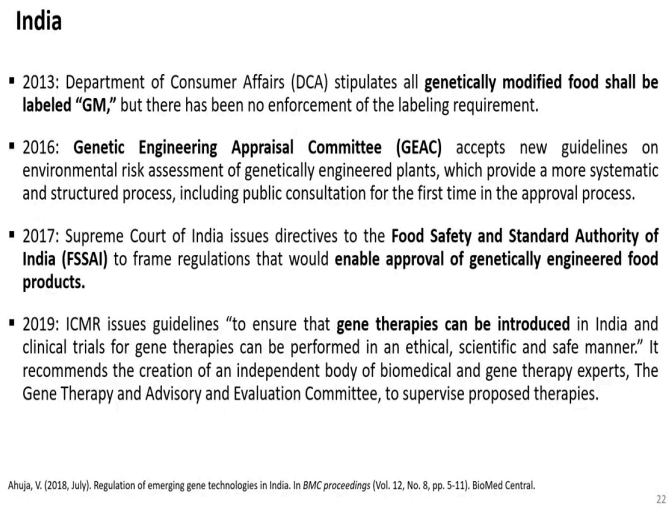

In 2013, department of Consumer Affairs stipulated that all genetically modified food shall be labeled as GM, but there has been no enforcement of the labeling requirement. In 2016, Genetic Engineering Appraisal Committee accepted new guidelines on environmental risk assessment of genetically engineered plants, which provide a more systematic and structured process, including public consultation for the first time in the approval process.

In 2017, Supreme Court of India issued directives to the Food Safety and Standard Authority of India to frame regulations that would enable approval of genetically engineered food products.

In 2019, ICMR issued guidelines to ensure that gene therapies can be introduced in India and clinical trials for gene therapies can be performed in an ethical, scientific and safe manner. It recommends the creation of an independent body of biomedical and gene therapy experts, the Gene Therapy and Advisory and Evaluation Committee, to supervise proposed therapies.

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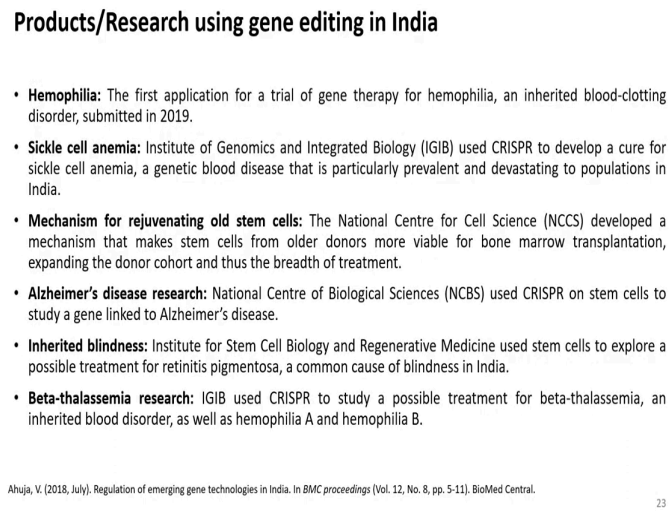

The products and research using gene editing in India hemophilia, the first application for a trial of gene therapy for hemophilia, an inherited blood clotting-disorder, was submitted in 2019. Institute of Genomics and Integrated Biology (IGIB) used CRISPR to develop a cure for sickle cell anemia, a genetic blood disease that is particularly prevalent and devastating to populations in India.

The National Centre for Cell Sciences developed a mechanism that makes stem cells from older donors more viable for bone marrow transplantation, expanding the donor cohort and thus the breadth of treatment. Alzheimer's disease research has also been accomplished the NCBS used CRISPR on stem cells to study a gene linked to Alzheimer's disease.

Institute of Stem Cell Biology and Regenerative Medicine use stem cells to explore a possible treatment for retinitis pigmentosa, a common cause of blindness in India. Institute of Genomics and Integrated Biology used CRISPR to study a possible treatment for beta-thalassemia an inherited blood disorder as well as hemophilia A and hemophilia B.

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Let us now examine some of the developments in this field in China. In 1993, Chinese ministry of public health released an outline of quality controls for clinical studies of human somatic and gene therapy. In 1999, Guiding Principles for Human Gene Therapy Clinical Trials were finalized.

In 2001, Regulations on the Administration of Agricultural Genetically Modified Organisms Safety was published, which heavily regulates the import and domestic production of genetically modified crops. In 2003, China's science ministry bans the implantation of genetically modified embryos for reproductive purposes and prohibits altered embryos developing past 14 days. No punishments are attached to the regulation.

The same year, Ministry of Health and Ministry of Science and Technology jointly develop the Ethical Principles of Research on Human Embryonic Stem Cells, which states that embryos derived by genetic modification must not be allowed to develop for more than 14 days and that once they have been used for research, they cannot be implanted into humans or other species.

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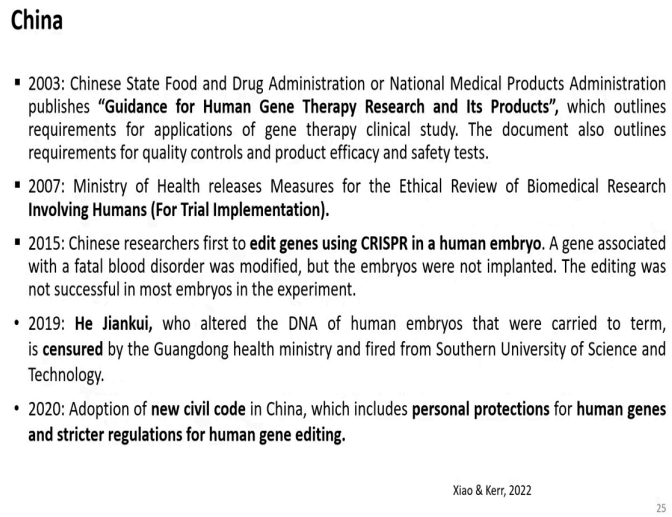

In 2003, Chinese State Food and Drug Administration or National Medical Products Administration published Guidance for Human Gene Therapy Research and Its Products, which outlines requirements for applications of gene therapy clinical study. The document also outlines requirements for quality control and product efficacy and safety tests.

In 2007, Ministry of Health released measures for the Ethical Review of Biomedical Research Involving Humans, for trial implementation. In 2015, Chinese researchers were the first to edit genes using CRISPR in a human embryo. A gene associated with a fatal blood disorder was modified, but the embryos were not implanted. The editing was not successful in most embryos in the experiment.

We have discussed about the case of He Jiankui, who altered the DNA of human embryos yesterday that were carried to term is censured by the Guangdong Health Ministry and was fired from the Southern University of Science and Technology, and was also later jailed and also his collaborators were also punished.

In 2020, adoption of new civil code in China, which includes personal protections for human genes and stricter regulations for human gene editing was initiated.

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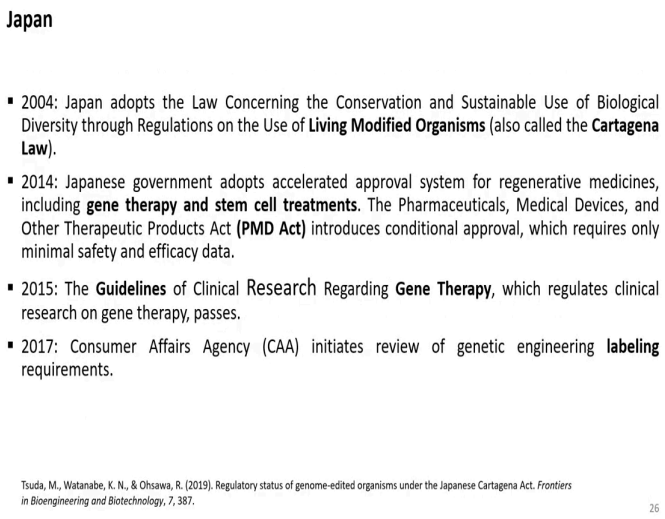

In the case of Japan in 2004 it adopted the Law Concerning the Conservation and Sustainable use of Biological Diversity through Regulations on the Use of Living Modified Organisms.

In 2014, Japanese government adopted accelerated approval system for regenerative medicines including gene therapy and stem cell treatments. The Pharmaceuticals, Medical Devices and other Therapeutic Products Act, PMD Act introduced conditional approval, which requires only minimal safety and efficacy data.

In 2015, The Guidelines for Clinical Research Regarding Gene Therapy, which regulates clinical research on gene therapy, was passed. In 2017, Consumer Affairs Agency initiated review of genetic engineering labeling requirements.

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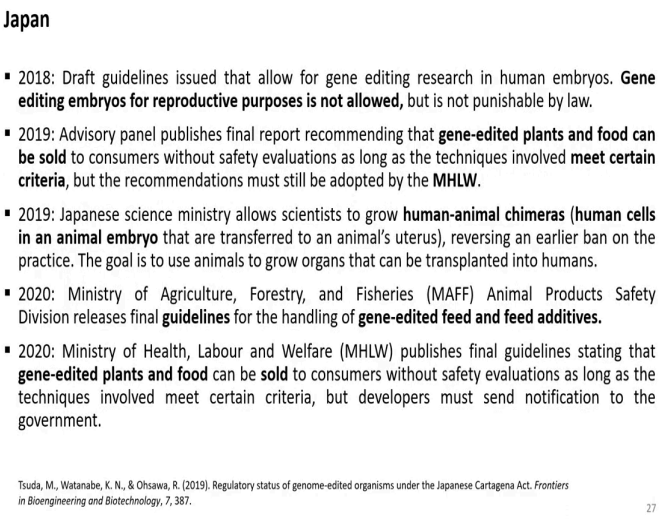

In 2018, the Draft guidelines were issued that allow for gene editing research in human embryos. Gene editing embryos for reproduction was not allowed, but is not punishable by law. In 2019, advisory panel publishes final report recommending that gene edited plants and food can be sold to consumers without safety valuations as long as the techniques involved meet certain criteria, but the recommendations must still be adopted by the MHLW.

In 2019, Japanese science ministry allows scientists to grow human-animal chimera's human cells in an animal embryo that are transferred to an animal's uterus, reversing an earlier ban on the practice. The goal is to use animals to grow organs that can be transplanted into the humans.

In 2020, Ministry of Agriculture, Forestry and Fisheries Animal Products Safety Division release the final guidelines for the handling of gene-edited feed and feed additives. The Ministry of Health, Labour and Welfare publish the final guidelines stating that gene-edited plants and food can be sold to consumers without safety evaluations as long as the techniques involved meet certain criteria, but developers must send notification to the government.

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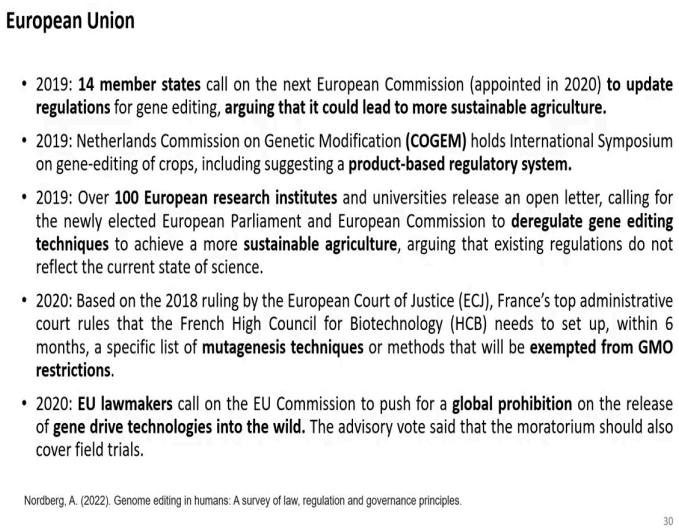

Let us now discuss about some of the developments in the European Union. In 2019, 14 member states call on the next European commission to update regulations for gene editing, arguing that it could lead to more sustainable agriculture. Netherlands Commission on Genetic Modification COGEM held international symposium on gene-editing of crops including suggestions of a product-based regulatory system.

Over 100 European research institutes and universities released an open letter calling for the newly elected European parliament and European commission to deregulate gene editing techniques to achieve a more sustainable agriculture, arguing that existing regulations do not reflect the current state of science.

In the same year based on the 2018 ruling by the European Court of Justice, France's top administrative court rule that the French High Council for Biotechnology needs to set up, within 6 months, a specific list of mutagenesis techniques or methods that will be exempted from GMO restrictions.

EU lawmakers call called on the EU Commission to push for a global prohibition on the release of gene drive technologies into the wild. The advisory vote said that the moratorium should also cover field trials.

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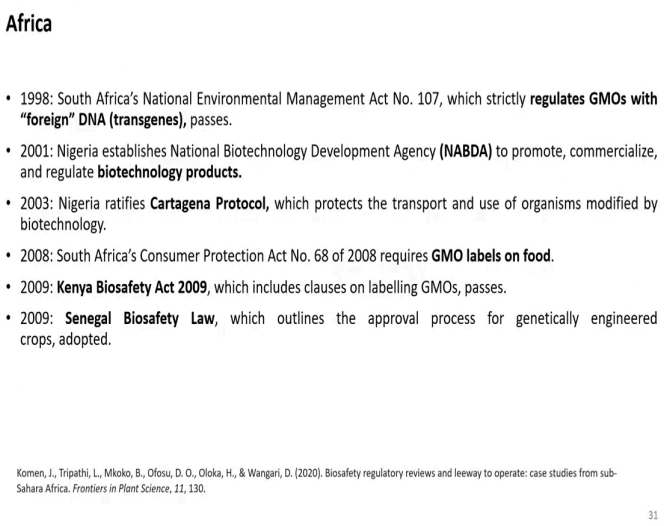

In Africa, also we can see various developments taking place from 1998 through the National Environmental Management Act number 107, which strictly regulated genetically modified organisms with foreign DNA.

In 2001, Nigeria establish National Biotechnology Development Agency to promote, commercialize, and regulate biotechnology products. And, they ratified the Cartagena Protocol, in 2003. And, in 2008 South Africa's Consumer Protection Act number 68 of 2008 was passed which required GMO labels on food.

And, 2009, Kenya Biosafety Act was passed which includes clauses on labeling GMOs and the Senegal Biosafety Law passed the same year also outline the approval process for genetically engineered crops.

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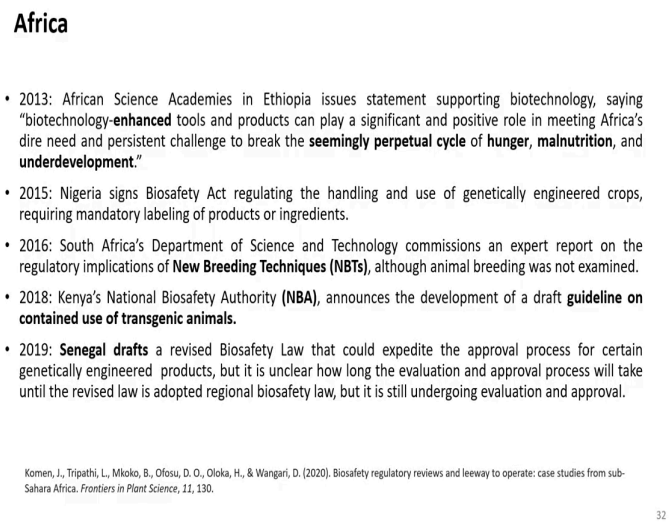

In 2013, African Science Academies in Ethiopia issued a statement supporting biotechnology, saying biotechnology-enhanced tools and products can play a significant and positive role in meeting Africa's dire need and persistent challenge to break the seemingly perpetual cycle of hunger, malnutrition and under development.

In 2015, Nigeria sign the Biosafety Act regulating the handling and use of genetically engineered crops, requiring mandatory labeling of products or ingredients. In 2016, South Africa's Department of Science and Technology commissions an expert report on the regulatory implications of New Breeding Techniques through animal breeding was not examined.

In 2018, Kenya's National Biosafety Authority announced the development of the draft guidelines on contained use of transgenic animals. In 2019, Senegal draft a revised Biosafety Law that could expedite the approval process for certain genetically engineered products, but it is unclear how long the evaluation and approval process will take until the revised law is adopted regional biosafety law, but it is still undergoing evaluation and approval.

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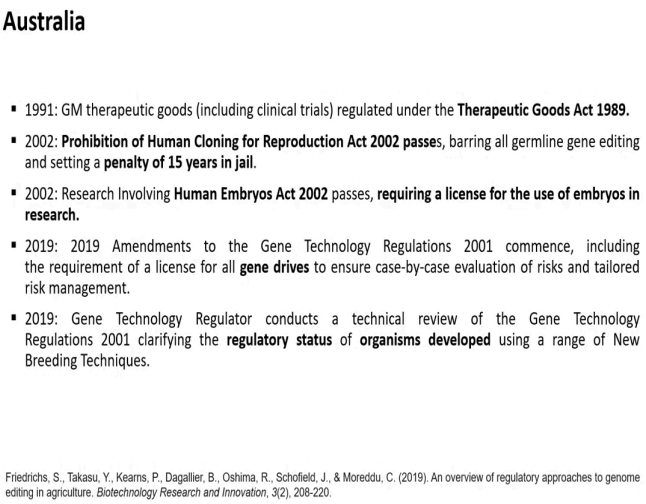

In Australia also, various developments regarding the regulatory landscape has taken place since 1991 when GM therapeutic goods regulated under the Therapeutic Goods Act 1989 come into action. In 2002, Prohibition of Human Cloning for Reproduction Act was passed barring all germline gene editing and setting a penalty of 15 years in jail.

In 2002, Research involving Human Embryos act 2002 was passed requiring a license for the use of embryos in research. In 2009, Amendments to the Gene Technology Regulations of 2001 were commenced, including the requirement of a license for all gene drives to ensure case-by-case evaluation of risks and tailored risks management.

Gene Technology Regulators conducts a technical review of the Gene Technology Regulations 2001 clarifying the regulatory status of organisms developed using a range of new Breeding Techniques.

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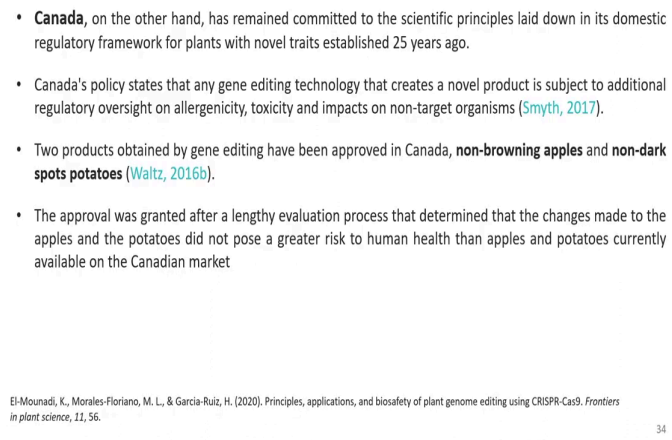

In the case of Canada, we can see it has remained committed to the scientific principles laid down in its domestic regulatory framework for plants with novel traits established more than 25 years ago. If the policy states that any gene editing technology that creates a novel product is subject to additional regulatory oversight of allergenicity, toxicity and impacts on non-target and impacts on non-target organisms.

Two products obtained by gene editing have been approved in Canada, non-browning apples and non-dark spots potatoes. The approval was granted after a lengthy evaluation process which determined the changes made to the apples and the potatoes and that they did not pose a risk to human health than apples and potatoes currently available on the Canadian market.

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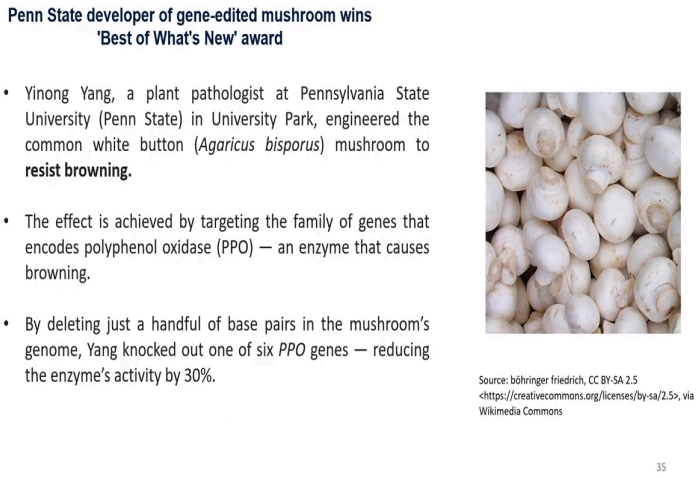

This is one interesting story about a Penn State developer who developed gene-edited mush room and he was awarded Best of What's New award. Yinong Yang, a plant pathologist at Pennsylvania State University in University Park, engineered the common white button *Agaricus bisporus* mushroom to resist browning. These mushrooms the normal ones the brown due to the shelf life they become brown and they lose the customers choice and they are they sell at a lower price.

So, by solving this browning problem, the quality of the product is sustained and so, is the income from selling these mushrooms. These browning was stopped by targeting the family of genes that encodes polyphenol oxidases – the enzyme which causes the browning. Yang deleted a handful of base pairs in the mushrooms genome and knocked out one of the six polyphenol oxidase genes – reducing the enzymes activity by 30 percent.

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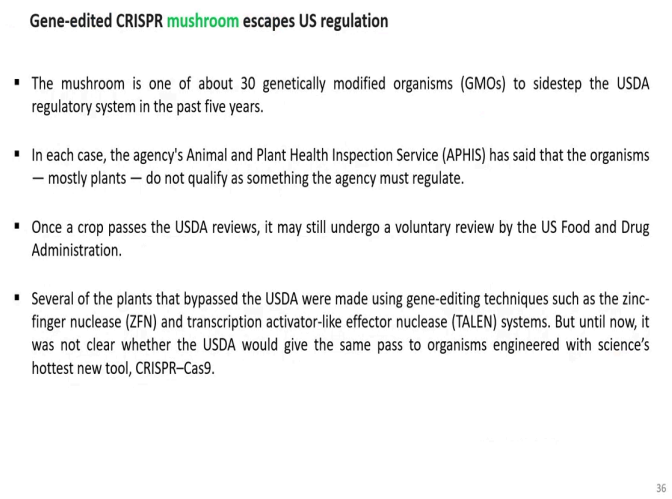

However, this is a very interesting case in terms of regulatory issues. These particular CRISPR edited mushroom escaped the US regulatory framework. The mushroom is one of about 30 genetically modified organisms which could sidestep the USDA regulatory system in the past decade in or five years.

In each case, the agency's Animal and Plant Health Inspection Service has said that the organisms which are mostly plants do not qualify as something the agency must regulate as per the existing guidelines and norms. Once a crop passes the USDA reviews, it may still undergo a voluntary review by the US Food and Drug Administration.

However, similar to plants that bypassed the USDA were made using gene editing techniques such as the as the zinc finger nucleus and TALEN. But until now, it was not clear whether the USDA would give the same pass to organisms engineered with science's hottest new tool, CRISPR-Cas9 until these CRISPR edited mushroom make it is way to the supermarket shelves.

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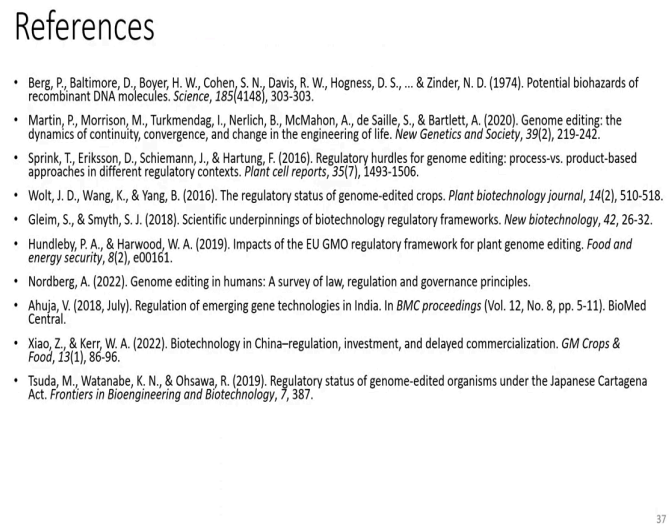

So, with this we come to end of these lecture under Module 12. These are some of the references which were used for preparing these lecture. Those who are interested, kindly refer to these original articles for any of the points or concepts where you may require little additional explanations or understanding.

Thank you for your patient hearing.