BETTER POLICIES FOR BETTER LIVES

ABSTRACTS

OECD Conference on Genome Editing

APPLICATIONS IN AGRICULTURE

Implications for Health, Environment and Regulation

28-29 June 2018

Abstracts

OECD Conference on Genome Editing:

Applications in Agriculture – Implications for Health, Environment and Regulation

Welcome Session

Gary Fitt – Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australia; Chair of the OECD Co-operative Research Programme Scientific Advisory Body

The OECD Co-operative Research Programme: Biological Resource Management for Sustainable Agricultural Systems (CRP) funds cutting-edge research on food, agriculture, fisheries and forestry with a focus on global issues such as sustainability, food security and nutrition, climate change and the inter-connectedness of economies through trade and scientific co-operation. The CRP helps achieve globally agreed policy objectives by facilitating international co-operation among research scientists and institutions. In doing so, it strengthens scientific knowledge and innovation.

With this focus on global issues, CRP-funded research generates benefits for people around the world. To deliver on these overarching challenges, the CRP has three themes into which funding proposals need to fit: Managing natural capital for the future; Managing risks in a connected world; Transformational technologies and innovation.

It achieves its objectives through two distinct activities:

- The CRP funds short-term research projects for individual scientists in other CRP member countries by providing travel bursaries to strengthen the exchange of ideas and increase international co-operation.
- The CRP sponsors international conferences and workshops to keep policy makers, industry and the academic world informed of innovative research, scientific developments and opportunities.

The CRP places a policy emphasis on all the activities it funds, and the findings from the activities provide valuable evidence and information to support policy makers in promoting the sustainable use of natural resources in food, agriculture, fisheries and forestry.

Find out more by visiting the CRP website: www.oecd.org/agriculture/crp.

Introductory Session

➢ Global perspectives in genome editing – Our genome-edited future: the promise and the challenge

Fyodor Urnov – Altius Institute for Biomedical Sciences, United States

The technology of genome editing with programmable nucleases (zinc finger, TAL effector, or Cas9-based) has clear potential for making a broad and positive impact worlwide. Evidence to this effect is provided by the rapid progress of genome editing from laboratory proof of concept (2001-2005) to its first successful use in the clinic, in crops, in human stem cells, cells used in biotechnology (2007-2009), and in agronomically and ecologically important animal, insect, and microbial species (2011). The application, in 2013, of Cas9 to genome editing has essentially eliminated the barrier between the investigator and a genetic outcome of interest in a cell or species of interest. This "democratization" of editing at the laboratory level then put into sharp focus the plethora of other challenges the technology faces. Clinical use of editing to date has targeted diseases with significant global impact: HIV, the hemoglobinopathies, and cancer. Here, the central goal, assuming a continued good record of safety and efficacy, is expanding the size of the patient population eligible for treatment (currently limited by logistics of clinical deployment and cost). Due to "safe harbor" provisions, intellectual property issues are not expected to adversely affect this effort, but a key clinical and ethical issue that needs to be addressed is editing as a disease prevention – rather than a treatment – modality, and the potential of "editing as enhancement." Applications of editing beyond the clinical space will face clear challenges of public acceptance, sustainability, and access; important precedent exists in biomedicine and biotechnology to create a framework in which to robustly address all of these.

➢ Global developments of genome editing in agriculture

Agnès Ricroch – AgroParisTech, France; College of Agricultural Sciences, Pennsylvania State University

Genome editing, particularly using of site-directed nucleases such as the CRISPR system, has spread rapidly through the biological sciences. Genome editing in crops could significantly speed up the progress of breeding programs. It could drive the development of traits in new crops and allow improvements in yield and pest resistance, adaptation to climate change, and industrial and pharmaceutical applications. However biofortification is a key challenge to satisfy nutritional needs in vitamins for developing countries and new consumer inquiries for developed countries. China and the USA take the lead in crop editing. Nigeria being headquarter to numerous research consortia is the most involved country in Africa. Genome editing in animals including pig, cattle, sheep, and carp, has not merely accelerated research but has made possible research that was previously unfeasible. It has been used to increase disease resistance, to make livestock better adapted to farming or environmental conditions, to increase fertility and growth, and to improve animal welfare. The USA, the UK and China are the most involved countries in animal genome editing. Global food production needs to increase as much as 70 per cent to support the growing population. Genome editing could contribute improving the efficiency of food distribution and reducing waste. Depending on the regulatory conditions, genome editing could open up the field to smaller companies and public labs.

Session 1: Genome editing applications in agriculture

➢ An overview of agricultural applications of genome editing: Crop plants

Caixia Gao – Institute of Genetics and Developmental Biology (IGDB), Chinese Academy of Science

Crop improvement requires the constant creation and use of new allelic variants. Conventional breeding can be limited in providing the genes and alleles required to meet the agricultural challenges. In the past decade, Genome editing can accelerate plant breeding by allowing the introduction of precise and predictable modifications directly in an elite background. The most promising utilization of both the CRISPR/Cas9 system can be used to generate targeted genome modifications including mutations, insertions, replacements and chromosome rearrangements. The use of CRISPR in agriculture should be considered as simply a new breeding method that can produce identical results to conventional methods in a much more predictable, faster and even cheaper manner.

➢ An overview of agricultural applications of genome editing: Farm animals

Simon Lillico – The Roslin Institute, University of Edinburgh

Selection based on phenotype has been the foundation of agricultural progress for centuries. While slow, this approach has resulted in multiple livestock breeds with unique characteristics associated with production or adaptive traits. Introducing beneficial traits from one breed into another requires crossing and subsequent backcrossing over a number of generations in order to capture the perceived benefit whilst maintaining the overall phenotypic merit of the original population. While relatively simple when a single gene variant underlies the trait, using this approach to introgress a phenotypic variant with a polygenic foundation is challenging. Application of genome editors allows the introduction of one or more specific genetic changes to an individual of high genetic merit in a single generation. As our understanding of genome/phenome interaction improves, we will be increasingly able to envisage the introduction of truly novel genetic variation, a feat that would not be possible with standard breeding regimes.

➢ Application of genome editing 1: Crop plants: DNA-free genome editing with CRISPR enzymes

Sunghwa Choe – School of Biological Sciences, College of Natural Sciences, Seoul National University

Processes of traditional trait development in plants depend on genetic variations derived from spontaneous mutation or artificial random mutagenesis. Limited availability of desired traits in crossable relatives or failure to generate the wanted phenotypes by random mutagenesis led to develop innovative breeding methods that are truly cross-species and precise. To this end, we devised novel methods of precise genome engineering that are characterized to use pre-assembled CRISPR/Cas9 ribonucleoprotein (RNP) complex instead of using nucleic ands or Agrobacterium. We found that our methods successfully engineered plant genomes without leaving any foreign DNA footprint in the genomes. To facilitate introduction of RNP into plant nucleus, we first obtained protoplasts after removing the transfection barrier, cell wall. Whole plants were regenerated from the single cell of protoplasts that has been engineered with the RNP. Pending the improved way of protoplast regeneration technology especially in crop plants, our methods should help develop novel traits in crop plants in relatively short time with safe and precise way.

➢ Application of genome editing 2: Crop Plants: Next-generation waxy corn - a flagship case of SDN-1/NHEJ genome editing via CRISPR/Cas9

Robert Meeley – Corteva Agriscience, DowDuPont

Genetic variants created by site-directed nucleases (SDN) are categorized as SDN-1, SDN-2 and SDN-3 depending on the outcome of DNA double strand break repair. This presentation gives a product development overview of Next Generation Waxy Corn hybrids for a targeted marketplace. Our strategy uses a dual guide-RNA, SDN-1, whole gene deletion approach, achieved via non-homologous end-joining (NHEJ) of the nuclease cut sites. Waxy corn starch is ~100% amylopectin starch that occupies a significant niche in the specialty corn market, with important food and industrial applications. Parallel editing of multiple inbred genotypes allows the rapid, precise creation of elite hybrid products with a significantly mitigated yield penalty - as compared to sister hybrids created using conventional genetic introgression methods. Next Generation Waxy Corn provides tangible opportunities to engage with international stakeholders on science-based regulatory policies for genome-edited agricultural products.

➢ Application of genome editing 3: Crop plants with improved culture and quality traits

Peter Rogowsky – ENS de Lyon, National Institute for Agricultural Research (INRA), France

The large French research project GENIUS (2012-2019, http://www.genius-project.fr/en/) is quite representative for the present status of the application of genome editing techniques to crop plants. It addresses a large variety of species (rice, wheat, maize, tomato, potato, oilseed rape, poplar, apple and rose), uses targeted mutagenesis as its work horse and is limited to proof of concept under confined conditions. It covers mainly traits linked to crop culture, such as disease resistance to viruses and fungi, flowering time, plant architecture, tolerance to salinity and plant reproduction but also traits improving the quality of agricultural products for industrial purposes. Examples are virus resistant tomato, early flowering apple and rose and low-amylose starch potato. Improved quality traits for food will be illustrated by the results from other labs that achieved low-gluten wheat, lycopene enriched tomato or high oleic soybean. The wide range of traits illustrates that genome editing has the potential to contribute to a more sustainable agriculture by the reduction of pesticides and the mitigation of climate change and to the bioeconomy by custom tailored quality traits.

➢ Application of genome editing 4: Crop plants with enhanced disease resistance

Vladimir Nekrasov – Rothamsted Research, United Kingdom

The presentation will give an overview of how the genome editing technology (CRISPR/Cas) can be applied for the purpose of improving disease resistance in crops in a way, which is faster and more precise as compared to the conventional breeding. The gene editing approach will be compared to the transgenesis one and a few examples will be given. The presentation will also address precision of CRISPR/Cas in plants and whether the off-targeting should be an issue of concern.

➢ Application of genome editing 5: The Global Need for Plant Breeding Innovation

Petra Jorasch – European Seed Association; International Seed Federation

The International Seed Federation (ISF) and its global seed and plant breeding sector continued to engage with governments and value chain stakeholders (including the grain trade) worldwide to promote science-based, consistent policy approaches to plant breeding innovation, especially around gene edited products. An underlying principle for determining these consistent criteria is:

Plant varieties developed through the latest breeding methods should not be differentially regulated if they are similar or indistinguishable from varieties that could have been produced through earlier breeding methods.

ISF collaborates with its members the national seed associations and cooperates with regional seed associations around the world as well as CropLife International and its global network to coordinate policy engagement and advocacy in priority geographies. The global seed industry has been encouraged to observe Argentina, Brazil, Chile, and soon Colombia adopting science-based, policies that facilitate innovation for both public and private plant breeders

ISF and its members continue to develop resources and content that highlights the need for and benefits of plant breeding innovation. Some of these infographics and videos can be found in the ISF resource bank at http://www.worldseed.org/our-work/plant-breeding/plant-breeding-innovation/#resource-bank that is constantly updated with new contents.

ISF has just adopted a position paper on Plant Breeding Innovation during its World Seed Congress in Brisbane, Australia. http://www.worldseed.org/wp-content/uploads/2018/06/Plant-breeding-innovation-Consistent-criteria-for-the-scope-of-regulatory-oversight.pdf

➢ Application of genome editing 6: Farm animals: Chicken

Mark Tizard – Genome Engineering Team, Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australia

The chicken is an exemplar of efficient intensive animal agriculture and provides two valuable food products, chicken meat and eggs. Only aquaculture is better, by efficiency, but poultry is still top, by mass, as global food animal products. However these benefits come with a number of challenges. The genetics of selective breeding have led to dramatic improvements in yield, efficiency and product quality, but the traits that relate to disease and welfare outcomes have not been so tractable. Both transgenics and genome editing have clear potential for impact in these two important areas but application of these technologies is complicated by the reproductive biology of birds. Techniques very specific to birds are required to achieve heritable (germline) edited traits. These are quite involved and, even though they now well-defined and reliable, advances are still likely. Currently the key targets for this technology are modifying chicken genes involved in virus-receptor interactions and cellular response involved in infection. For the egg industry the technology is being applied to the issue of sex-selection for layer hens (and the removal of males), removal of egg allergens and the tailoring of eggs system to enhance the production of influenza vaccine doses. Regulation and trading of the animals generated, and resulting food products, will significantly impact the value of and future developments in genome editing of poultry

➢ Application of genome editing 7: Farm animals: Cattle

Alison Van Eenennaam – Department of Animal Science, University of California, Davis

Milk and meat from cattle and buffaloes contributes 45% of the global animal protein supply, followed by chickens (31%), and pigs (20%). In 2016, the global cattle population of 1.5 billion head produced 6.5 billion tons of cows' milk, and 66 million tons of beef. In the past century, cattle breeding programs have greatly increased the yield per animal with a resultant decrease in the emissions intensity per unit of milk or beef, but this has not been true in all regions. Genome editing research in cattle to date has focused on disease resistance (e.g. tuberculosis), production (e.g. myostatin knockout; production of all-male offspring), elimination of allergens (e.g. beta-lactoglobulin knockout) and welfare (e.g. polled or hornlessness) traits. Modeling has revealed how the use of genome editing to introduce beneficial alleles into cattle breeds could maintain or even accelerate the rate of genetic gain accomplished by conventional breeding programs, and is a superior approach to the lengthy process of introgressing those same alleles from distant breeds. Genome editing could be used to precisely introduce useful alleles (e.g. heat tolerance, disease resistance) and haplotypes into native locally-adapted cattle breeds, thereby helping to improve their productivity. As with earlier genetic engineering approaches, whether breeders will be able to employ genome editing in cattle genetic improvement programs will very much depend upon global decisions around the regulatory framework and governance of genome editing for food animals.

➢ Application of genome editing 8: Farm animals in aquatic systems

Anna Troedsson-Wargelius – Institute for Marine Research, Norway

Gene editing offers opportunities to solve major fish farming sustainability issues that are at present hampering expansion of the industry. In for example salmon farming, there are now two major bottlenecks limiting the expansion of the industry. One is the genetic impact of escaped farmed salmon on wild populations, which is considered the most long-term negative effect on the environment. Secondly and the utmost acute problem is the fish parasite salmon lice, which is currently causing high lethality in wild salmonids due to high concentrations of the parasite in the sea owing to sea cage salmon farming. There are also sustainability issues associated with the increased use of vegetable-based ingredients as replacements for marine products in fish feed. This transition comes at the expense of the omega-3 content both in fish feed and the fish filet of the farmed fish. Reduced fish welfare represents another obstacle, and robust farmed fish is needed to avoid negative stress associated phenotypes such as cataract, bone and fin deformities, precocious maturity and higher disease susceptibility. Gene editing could solve some of these problems and we can now produce sterile fish by gene editing and we have also altered the omega-3 content in the filet.

Session 2: Risk and safety considerations

➢ Current risk assessment approaches for environmental and food & feed safety

Jeffrey D Wolt – Biosafety Institute for Genetically Modified Agricultural Products (BIGMAP); Crop Bioengineering Center, Iowa State University

Foundational activities at the international level underlie current risk and safety assessment approaches for genetically engineered/modified organisms (GEOs/GMOs). Early risk assessment considerations beginning with the OECD 'Blue Book' established risk/safety assessment as the characterization of the organism and its environmental release; establishment and persistence in the environment; and human and ecological effects, analyzed in principle through existing methods. Important in this context was recognition that GEOs/GMOs as a class did not represent new risks relative to products of traditional plant breeding and that any incremental risk would need to be established on a stepwise case-by-case comparative basis with existing crops and derived-foods as the baseline. Accordingly, concepts of familiarity and substantial equivalence were advanced by OECD and Codex as ways to establish a risk analysis baseline for determining whether and to what extent risk/safety assessment was needed. Regulatory implementations of this paradigm have skewed to increasingly complex portfolios of studies rather than adhering to analysis which is formulated to fit the risk/safety questions relevant to a given case. Plants produced through genome editing technology will benefit from risk analysis that implements sound problem formulation to guide the need for and nature of risk/safety assessments.

➢ Genetic variations and potential risks – Traditional breeding and genome editing

Yutaka Tabei – Institute of Agrobiological Sciences, National Agriculture and Food Research Organization (NARO), Japan

Japanese Government started the Cross-ministerial Strategic Innovation Promotion Program including a research program of genome editing in 2014. This program aims to develop new methods for genome editing and new varieties of crops. In addition, this project includes the collection of scientific information for science communication about genome editing. Public concerns are apt to be directed to the new and inherent risks of new technology. In order to show whether there is any inherent risk in plants produced by genome editing, we determined the basal levels of mutational frequency in breeding techniques such as conventional mutation breeding, tissue culture, genetic transformation and genome editing. Based on the results, we conclude that there is no significant difference in the occurrence of genetic mutations among genome editing, genetic transformation and tissue culture.

➢ Considerations of unintended effects in genome editing applications

Marie-Bérengère Troadec – Institute of Genetics and Development of Rennes (IGDR), National Center for Scientific Research (CNRS), France

Agriculture has benefited from conventional plant breeding techniques, including chemical- or radiation-induced mutagenesis, and transgenesis. Genome editing techniques are likely to allow straightforward, cost-effective and efficient gene-specific modifications of agronomic interest. As for previous plant breeding techniques, genome editing techniques may be associated with unintended effects. Evaluation of potential novel risks associated with genome editing must be considered. Using a broad theoretical approach, three categories of safety considerations for health and the environment were identified, as compared to conventional breeding : (1) risks due to unintended effects on the end product inherent to genome editing techniques — including unintended effects associated with effector persistence as well as risks associated with off-target modifications and other unintended genome modifications —, (2) risks arising from the desired traits and their novelty in the plant, and (3) risks associated with potential acceleration of plant breeding, owing to efficiency and technical ease of use of genome editing, be it for single traits or for combined modifications (multiplex genome editing). The potential need for evolution of current risk assessment and management must be discussed. Based on High Council for Biotechnology experience, the possible impacts and weigh of these different safety considerations on risk assessment will be presented.

Session 3: Regulatory aspects

Country 1: Argentina

Martin Lema – Secretariat of Foodstuff and Bioeconomy, Ministry of Agro-Industry; National University of Quilmes

The Argentine Republic has accumulated vast experience in the regulation and use of Genetically Modified Organisms for agroindustrial purposes. In particular, the regulatory aspects of gene editing applied to agriculture were considered proactively, and a simple but sound pioneer regulation was developed.

The Argentine regulatory system is now able to establish if a gene-edited crop, animal or microorganism should be classified and handled either as a GM crop or a conventional new variety/breed/line/strain. To this end, the concept of "novel combination of genetic material" resulting from the Cartagena Protocol has been of utmost importance, although other factors have shaped this regulation and are applied on its implementation.

After some pilot cases that have been handled under the new regulation, applicants appreciate the ease, speed and predictability of this regulation. Moreover, it has been considered by other countries in developing their own policies, thus helping also to harmonize the insertion of these technologies in the global market.

Country 2: Australia

Peter Thygesen[1] and Lisa Kelly[2] – [1] Office of the Gene Technology Regulator (OGTR); [2] Food Standards Australia New Zealand (FSANZ)

In Australia, oversight of genetically modified organisms (GMOs) is provided by the Gene Technology Act 2000 (GT Act), administered by the Office of the Gene Technology Regulator (OGTR) to manage any risks posed to people or the environment. The GT Act operates in conjunction with other Australian regulations for human food, human therapeutics, veterinary medicines and agricultural chemicals. GM food products are regulated separately under the joint Australia and New Zealand food regulation system through the Australia New Zealand Food Standards Code (the Code) administered by Food Standards Australia New Zealand (FSANZ), specifically Standard 1.5.2 Food produced using gene technology (adopted in 1999).

There has been ongoing uncertainty in Australia about whether genome editing techniques are captured by current legal definitions in regulations for GMOs and GM food, e.g. definitions of 'gene technology', 'GMO', and 'food produced using gene technology' in the GT Act and the Code. The presentation will discuss work being undertaken in Australia to clarify the regulation of genome editing under GMO and GM food legislation, including in the light of current scientific knowledge (see
www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/reviewregulations-1 and
www.foodstandards.gov.au/consumer/gmfood/Pages/Review-of-new-breeding-technologies-.aspx).

Country 3: Canada

Christine Tibelius – Plant Health Science, Canadian Food Inspection Agency

Canada's regulatory framework is based on the novelty of the product, not the process by which the product was developed. Therefore the regulatory focus is on the novel trait of the product regardless of the method used to introduce the trait. The Canadian Food Inspection Agency is responsible for the regulation of the environmental release of plants with novel traits, and novel animal feeds, while Health Canada is responsible for the regulation of novel foods. In all cases, these novel products may be the result of mutagenesis, recombinant DNA techniques or other methods of plant breeding such as gene editing. This novelty approach allows the Canadian regulatory system to efficiently adjust to any new developments in the science of plant breeding and allows for risk-appropriate regulatory decisions. This approach encourages innovation while maintaining science-based regulatory expertise. Canadian regulators work cooperatively with proponents to determine if their gene editing-derived plant product meets the definition of a novel product, and whether it would be subject to a pre-market safety assessment. Therefore, Canada's existing regulatory system is well positioned to accommodate any new innovations or technologies in plant breeding, including gene editing.

Country 4: European Union

Chantal Bruetschy – Unit "Biotechnology", European Commission

Genome editing techniques are attracting increasing interest as a tool to alter the genetic material of living organisms. They can be used in many different ways on many different species, to obtain different types of organisms, with different genetic properties and traits. The use of these new technologies has great potential to address societal needs. Yet, safety, ethical, animal welfare and environmental considerations should be taken into account in using these techniques.

As in many countries of the world, one of the questions in the EU concerns the regulatory framework applicable to the organisms and products obtained with genome editing techniques. The EU has extensive legal framework in many sectors, including GMOs, ensuring high safety standards and effective functioning of the internal market. Whether genome editing techniques lead to products falling under the EU GMO legislation is currently under the scrutiny of the Court of Justice of the EU.

In a rapidly changing world, the challenge for governance is to reinforce and foster responsible innovation while maintaining high safety standards, transparent communication and freedom of choice for economic operators including consumers. A wide range of actors (researchers, companies, NGOs, policy makers, traders) have to contribute to these objectives as they all have an important role to play and a joint responsibility in the governance of new technological developments.

Country 5: India

Murali Krishna Chimata – Ministry of Environment, Forest and Climate Change

In India, genetically modified organisms (GMOs) and products thereof are regulated under the "Rules for the manufacture, use, import, export & storage of hazardous microorganisms, genetically engineered organisms or cells, 1989" (referred to as Rules, 1989) notified under the Environment (Protection) Act, 1986. These Rules are implemented by the Ministry of Environment, Forest and Climate Change, Department of Biotechnology and State Governments though six competent authorities. The Rules, 1989 are supported by series of guidelines on contained research, biologics, confined field trials, food safety assessment, environmental risk assessment etc.

The definition of genetic engineering in the Rules, 1989 implies that new genome engineering technologies including gene editing technologies like CRISPR/Cas9 and gene drives may be covered under the rules. India is a signatory to the Cartagena Protocol on Biosafety (CPB), however, the definition of modern biotechnology, as in CPB is yet to be adopted in the national regulations. The regulatory authorities review and take into account the experience by other countries in dealing with new technologies. However, there is yet no clarity on how the emerging technologies will be dealt with in India, though research has been initiated in several leading institutions.

Country 6: United States

Sally McCammon[1], Kathleen Jones[2] and Mike Mendelsohn[3]– [1] Animal and Plant Health Inspection Service (APHIS), US Department of Agriculture (USDA); [2] Center for Veterinary Medicine (CVM), US Food and Drug Administration (FDA); Biopesticides and Pollution Prevention Division, U.S. Environmental Protection Agency (EPA)

The policy of the United States Government is to seek regulatory approaches, consistent with applicable laws, that protect health and the environment while reducing unnecessary regulatory burdens and avoiding unjustifiably inhibiting innovation, stigmatizing new technologies, or creating unnecessary trade barriers. U.S. agencies are focused on: maintaining high standards based on the best available science and delivering appropriate health and environmental protection; establishing transparent, coordinated, predictable, and efficient regulatory practices across agencies with overlapping jurisdiction; and promoting public confidence in the oversight of the products of biotechnology through clear and transparent public engagement. U.S. agencies that regulate the products of agricultural biotechnology will discuss their regulatory approaches, focusing on plants and animals developed using genome editing.

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