Gene Edited Crops – Need for Rationalized and Proportionate Risk Assessment and Regulation

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Corteva

Purpose

To enrich the lives of those who produce and those who consume, ensuring progress for generations to come.

Crop Protection & Nitrogen Management Solutions

Germplasm, Traits, and Seed Applied Technology

Natural Products & Biologicals

Digital Solutions
Same Breeding Goals - Now with a Better Tool

Evolution of Precision Breeding

- Inherent variability (chemical, X-ray mutagenesis)
- Induced variability
- Marker assisted selection
- Gene editing

Key benefits:
- Knowledge
- Efficiency
- Specificity

Cost and Development:
- Time
- Cost
Gene Editing – Applications

Precise, yet flexible, set of tools allowing to make specific, targeted improvements to plant genomes

- DNA Bind
- DNA Cut
- DNA double strand break (DSB) at nuclease target site
- Repair template
- OFF SDN-1
- EDIT SDN-2
- INSERT SDN-3
Gene Editing Possibilities for Farmers

<table>
<thead>
<tr>
<th></th>
<th>WHEAT</th>
<th>STRAWBERRIES</th>
<th>CORN</th>
<th>SOY</th>
<th>CANOLA</th>
<th>RICE</th>
<th>SUNFLOWER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease resistance</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Higher yield using fewer resources</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Drought tolerance</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Better product quality</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Faster to mature</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td>Slow browning or rot</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<td>✓</td>
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</tr>
</tbody>
</table>
Gene Editing Possibilities for Consumers

- Enhance heart-healthy soybean oil
- Create low-gluten wheat (targeting proteins associated with celiac and gluten sensitivity)
- Improve the flavor and cost of decaffeinated coffee with a naturally decaffeinated bean
- Boost the cocoa plant’s immune system to resist a harmful virus
- Reduce vineyard fungus affecting the wine industry
- Protect bananas against disease
- Shield oranges from a disease decimating citrus orchards
Opportunities for Global Agriculture

- Targeted plant breeding
- Variety of potential applications across value chain
- Opportunities for polyploid crops and crops with limited genetic diversity
- Rate of the technology adoption impacted by proportionality of the regulatory regime
Plant Breeding Develops Product Diversity

Plant breeding utilizes **genetic variation** to develop new varieties with useful characteristics.
Spontaneous Genetic Diversity in Plants

Inherently occurring genome editing processes are fundamental to crop adaptation and the successful development of high performing elite varieties.

**Single Nucleotide Polymorphism (SNP)**

Soy
1.8 mln novel SNPs in 1 ha field


**Gene Copy Number Variation (CNV), Presence/Absence Variation (PAV)**

Tannat grape
1873 genes not shared with the grape reference genome


“Any 2 maize varieties differ from one another in 1.4% of their DNA... This level of nucleotide diversity is...14 times higher than that of humans...the divergence between 2 maize lines is approximately equivalent to the difference between humans and chimpanzees.”

Genetic Diversity Is Greatly Induced by Traditional Mutational Breeding

>3,200 varieties

Officially released mutant crop varieties by crop type and usage (2013)

Mutant crop varieties by geography (2013)

Long history of safe use!

Gene Editing: Evolution of Precision Breeding

Continues the history of crop improvement through **targeted** breeding approach

**MUTATIONAL BREEDING**

Untargeted  

Targeted  

Targeted mutagenesis approach, now offered by gene editing tools, dramatically increases the efficiency of plant breeding

desired mutation  

agronomic evaluations  

desired trait
Plant breeders utilize well-established evaluation and selection practices to advance lines containing favorable characteristics.

**Example of Maize**

**INBREDS** > 30 traits

**HYBRIDS** > 40 traits

such as:

- Vegetative characteristics
- Ear photometry
- Yield
- Disease resistance
- Certification traits

Several years of comprehensive multi-location field evaluations according to common breeding practices.
Global Regulatory Policies for Gene Editing (September, 2019)

- **Canada**
- **U.S.**
- **Brazil**
- **Chile**
- **Argentina**
- **Honduras**
- **Panama**
- **Colombia**
- **Paraguay**
- **Uruguay**
- **S. Africa**
- **EU**
- **Israel**
- **Paraguay**
- **Taiwan**
- **China**
- **Japan**
- **Philippines**
- **Australia**
- **Uruguay**
- **New Zealand**

**Legend:**
- **Green** - in place
- **Blue** - in development
- **Red Outline** - policy developments since November, 2017
Case-by-Case Consultation Frameworks in Latin America

In development:
- Honduras
- Panama
- Uruguay

- Case-by-case consultation process for non-GMO confirmation
- Science-based approach in alignment with the country’s legislation, GMO definition, and in alignment with the Cartagena Protocol for Biodiversity’s LMO definition.
- Not a GMO if no novel combination of genetic material that could be obtained only by modern biotechnology
  - Molecular data to confirm absence of foreign DNA
- Efficient: review and response in 20-90 business days
- Promoting and encouraging innovation
Organisms obtained by mutagenesis are GMOs and are, in principle, subject to the obligations laid down by the GMO Directive.

However, organisms obtained by mutagenesis techniques which have conventionally been used in a number of applications and have a long safety record are exempt from those obligations, on the understanding that the Member States are free to subject them, in compliance with EU law, to the obligations laid down by the directive or to other obligations.

- Court’s reasoning for strict interpretation – Precautionary Principle
  “…the precautionary principle was taken into account in the drafting of the directive and must also be taken into account in its implementation.”

- Court acknowledged the inherent limitations in the posture of the scientific information before the Court

- Court did not apply its ruling to any particular product or technique/method

- The scientific information before the Court did not acknowledge that identical products, with the same safety profile, could be created through traditional breeding, including conventional mutagenesis techniques.
Legal Consequences of the ECJ Ruling

- Unjustified use of the EU precautionary principle
  - More hazard-based than risk-based approach

- Process, and not product-based approach
  - Like products will be regulated differently

- Diverging from non-EU countries

- Challenges with detection methods

- Lingering uncertainties

"Most of the mutations induced by genome editing technologies cannot be unequivocally distinguished from natural mutations"…<and>

"can currently not be differentiated from those induced by conventional mutagenesis techniques, which have been incorporated in traditional breeding programs and are often not thoroughly documented".

Gene Editing - Risk and Safety Considerations

- Learnings from GMO
  - History of risk and risk assessment approaches
  - Current risk assessment and safety assessment approaches

- LMO as per Cartagena Protocol
  - ... organism that possess a novel combination of genetic material obtained through ... in vitro rDNA techniques...
  - What is ”novel combination of genetic material”?

- “GMO” in the regulatory context is an organism that possesses a novel combination of genetic material that is possible only by modern biotechnology (i.e., impossible to find in nature or obtain through conventional breeding)

- What should be the risk and safety considerations when gene edited products do not contain novel combination of genetic material?
What is the appropriate policy framework to facilitate innovation while protecting human health and the environment?

- Science-based, accommodate new evidence and learning

- Risk-proportionate:
  - Cost effective and commensurate with the risk
  - Regulatory oversight for the two identical products should be no different

- Transparent, consistently applied and enforced

- Globally harmonized

- Promoting innovation to address local and global agricultural challenges
“Plant varieties developed through the latest plant breeding methods should not be differentially regulated if they are similar or indistinguishable from varieties that could have been produced through earlier plant breeding methods”
Potential implications of asynchronous regulatory requirements for pre-market assessment of gene edited products

- Limit the innovation
- Negatively affect research collaborations
- Hinder the movement of seed globally
- Potential impact to trade
- Enforcement issues
- Cost and time escalation for product approval
- Might cause public distrust
“GMO” in the regulatory context is an organism that possesses a novel combination of genetic material that is possible only by modern biotechnology (i.e., impossible to find in nature or obtain through conventional breeding).

Existing regulatory frameworks are adequate to address products of gene editing techniques.

- If gene-edited organism could not be obtained through conventional breeding or found in nature, existing GMO regulatory frameworks apply.
- If gene-edited organism could be obtained through conventional breeding or found in nature, it should be regulated similarly to conventionally-bred products – considered non-GMO.
Conventional breeding utilizes both spontaneous and induced mutations

• It has a solid track record of safe use (development of varieties that are safe for human and animal health, and the environment)

• Prior to commercialization, conventional varieties undergo extensive agronomic evaluations; lines with beneficial characteristics are selected

Gene editing is targeted breeding that can have much lower frequency of unintended changes, compared to conventionally-bred products

• Same evaluation and selection processes yet apply to non-GMO gene-edited varieties as to conventional varieties
Thank you

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