Regulation of GE Trees in the U.S. and Beyond

Are Forest Trees Treated Differently?

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The National Academies of Sciences, Engineering, and Medicine

March 8, 2018
Discussion Topics

1. **Status**: How & why GE trees are regulated.

2. **Challenge**: Obstacles to unmanaged use of GE trees in the wild.

3. **Opportunity**: Forest health and new technologies can push regulations in bold new directions.
US Statutory & Legal Considerations

**APHIS** Regulation triggered by plant pest use (but using disarmed agrobacterium is effectively a process today)
- Q: What is the effect of the plant on the environment?

**EPA** regulates if there is a Plant Incorporated Protectant (PIP) under Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
- Q: How will a PIP affect the environment and be managed?

**FDA** regulates if the plant produces food for people or animals
- Q: How different is the GE product from a non-GE?

**NEPA** National Environmental Policy Act requires:
- Environmental Assessment (EA) *quicker/easier* OR
- Environmental Impact Statement (EIS) *slower/harder*

**Tort law**
- Civil harm resulting in lawsuits – organic growers in particular

**Fun Fact:** NEPA requires agencies to assess the significance of an action in several contexts such as social (human, national), affected parties, and geographic regions.
The U.S. GE regulatory system is based on risk assessment, but it's inadequate. Consider:

- A plant pest (according to 7 CFR 340) triggers GE regulation - even when combatting a plant pest. Ironic or flawed?

- No mechanism for addressing the risk of inaction/slow action that is $>>>$ greater than rapid action with some uncertainty.

- Unregulated biotechnologies may create a very similar product but have no oversight or risk assessments.

- GE gene flow to native populations is historically considered undesirable. No good model for it being a desired outcome.
All GE Plants are = Once ‘Deregulated’

- Once a GE plant is given ‘Non Regulated’ status by APHIS, it’s treated the same as any other GE plant.
  - A plant’s ‘Non Regulated’ status can be rescinded (regulated) in light of new information.

- The EPA regulates PIPs in EACH plant, ostensibly uniquely. Typically doesn’t stop regulating, just licenses.
  - Gene flow & introgression into wild population will be considered.
  - Chain of custody issues when genes are intended to introgress.

- FDA doesn’t strictly regulate GE plants, just stops asking for more info when satisfied it is safe.
  - Corollary ‘deregulation’ approach as APHIS (once considered safe, it’s treated same as any other GE plant)
Getting to ‘Deregulated’ is Different for GE Trees

Originally designed to handle GE crops, regulations aim to determine “what will it do do & where will it go?” with:

1. Information throughout the lifecycle of a plant
   - Trees change as they age, and live a long time
   - Permits typically renewed every 3 years

2. Physical containment for gene control
   - Trees get big

3. Flower/pollen control
   - Trees may not flower for years
   - How to satisfy #1 without open pollination?

4. Limited acreage (EPA requires an Experimental Use Permit (EUP) for > 10 cumulative acres of field trials)
   - 10 acres of corn ~ 250,000 stalks vs ~5,000 trees (50x fewer trees)
   - Plantings in different provenances required to satisfy requirement #1
## Regulatory System Assessment

<table>
<thead>
<tr>
<th>Country</th>
<th>Biotech Framework</th>
<th>Primary Agency</th>
<th>GE Tree specific Regs.</th>
<th>Cartagena Signatory</th>
<th>Stringency Score*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>Yes</td>
<td>National Biosafety Technical Commission (CTNBio)</td>
<td>No</td>
<td>Yes</td>
<td>50</td>
</tr>
<tr>
<td>Chile</td>
<td>No</td>
<td>NA</td>
<td>No</td>
<td>No</td>
<td>NP (35)</td>
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<tr>
<td>Uruguay</td>
<td>Yes</td>
<td>National Biosafety Commission (GNBio)</td>
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<td>Yes</td>
<td>25</td>
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<tr>
<td>U.S.A.</td>
<td>Yes</td>
<td>Animal and Plant Health Inspection Service (APHIS)</td>
<td>No</td>
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<td>35</td>
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<tr>
<td>Canada</td>
<td>Yes</td>
<td>Canadian Food Inspection Agency (CFIA)</td>
<td>No</td>
<td>No</td>
<td>30</td>
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<tr>
<td>S. Africa</td>
<td>Yes</td>
<td>Department of Agriculture, Forestry, and Fisheries (DAFF)</td>
<td>No</td>
<td>Yes</td>
<td>30</td>
</tr>
<tr>
<td>China</td>
<td>Yes</td>
<td>Ministry of Agriculture (MOA) for agriculture, State Forestry Administration (SFA) for biotech trees</td>
<td>Yes</td>
<td>Yes</td>
<td>50</td>
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<tr>
<td>N. Zealand</td>
<td>Yes</td>
<td>Ministry of Agriculture and Forestry (MAF)</td>
<td>No</td>
<td>Yes</td>
<td>65</td>
</tr>
</tbody>
</table>

* Research by Vigani, Raimondi, and Olper at University of Milan, Italy. Uruguay assessed by the IFB, verified by Vigani.

NP = No commercial GE Products
Brazil Vs US Timelines

GE Eucalyptus trees petitioning for commercial deregulation

• FuturaGene submitted deregulation petition to CTNBio in January 2014
  - Commercial approval was granted April 2015
  - Process took 15 months

• ArborGen submitted a petition for non-regulated status in January 2011
  - 85 months after submission the EIS is still pending
USDA-APHIS is GE regulatory lead triggered by use of plant pest, but agrobacterium as a transformant is disarmed – not a pest, just a process technology. Consider a GE American chestnut developed with:

- Chinese Chestnut genes using Disarmed Agrobacterium
  = **No New** Proteins & **Regulated** by USDA

- Wheat genes using Biolostics
  = **New** Proteins & **Not Regulated** by USDA

- Gene editing (i.e. Crispr) can edit, remove, or add DNA
  = **New** Proteins & **Not Regulated** ???

Will the lack of up to date, science-based regulation increase public distrust of GE products?
## What is Subject to EU/Cartagena Regulation?

<table>
<thead>
<tr>
<th>Technique</th>
<th>YES/NO</th>
<th>Why?</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDN1-1 and 2 (site directed nucleases)</td>
<td>NO</td>
<td>Conventional mutagenesis (EU), the alteration could occur naturally</td>
</tr>
<tr>
<td>SDN-3 (non-foreign genes)</td>
<td>NO</td>
<td>The alteration can occur naturally</td>
</tr>
<tr>
<td>SDN-3 (foreign genes)</td>
<td>YES</td>
<td>Incorporates additional genetic material, the alteration cannot occur naturally</td>
</tr>
<tr>
<td>ODM (oligonucleotide-directed mutagenesis)</td>
<td>NO</td>
<td>Precision mutagenesis (EU), the alteration could occur naturally</td>
</tr>
<tr>
<td>Cisgenesis</td>
<td>NO</td>
<td>The alteration could occur naturally</td>
</tr>
<tr>
<td>Reverse breeding*</td>
<td>NO</td>
<td>There is no genetic alteration</td>
</tr>
<tr>
<td>RdDM* (RNA-directed DNA methylation)</td>
<td>NO</td>
<td>There is no change in the order of the genetic material</td>
</tr>
</tbody>
</table>

ZFN, TALEN and CRISPR/Cas9 are all site directed nucleases (SDN)

*Intermediate products may be within the scope of the GMO legislation

No official EU position yet. EU will develop ‘interpretation guidance document’
## (Best Guess) Legal Status Outside of EU

<table>
<thead>
<tr>
<th>Country</th>
<th>SDN-1</th>
<th>SDN-2</th>
<th>SDN-3</th>
<th>ODM</th>
<th>Cisgenesis</th>
<th>Reverse breeding</th>
<th>RdDM</th>
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<tbody>
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<td>Regulated</td>
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<td>CBC, Regulated</td>
<td>CBC, Regulated</td>
<td>CBC, Regulated</td>
<td>NS</td>
<td>Regulated</td>
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<td>CBC</td>
<td>CBC</td>
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<td>-</td>
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<tr>
<td>Canada</td>
<td>Yes, if PNT</td>
<td>Yes, if PNT</td>
<td>Yes, if PNT</td>
<td>Yes, if PNT</td>
<td>Yes, if PNT</td>
<td>NS</td>
<td>Yes, if PNT</td>
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<tr>
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<td>-</td>
<td>-</td>
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<td>Regulated</td>
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<tr>
<td>New Zealand</td>
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<tr>
<td>USA</td>
<td>CBC, NS</td>
<td>CBC, NS</td>
<td>CBC, Regulated, if PIP (EPA)</td>
<td>-</td>
<td>Regulated if agrobacterium is used (APHIS)</td>
<td>NS</td>
<td>-</td>
</tr>
</tbody>
</table>

CBC = Case-by-Case | NS = Not Subject to Legal Provisions | PIP = Plant Integrated Pesticide | PNT = Plant with Novel Trait

Compiled with input from: Dr. René Custers – VIB Belgium
Stakeholder Driven Stewardship of GE Trees

IF unmanaged GE trees can be safely released AND their benefit outweighs any risks, HOW can they be used when:

- Trees migrate yet regulations are inconsistent around the world
- GE technologies move fast and are not always regulated, even if scientific and public consensus concludes they should be
- Stakeholders feel left out, unheard, harmed, and misled

**IFB’s Response:** Stakeholder developed Principles that are consistent, global, science-based, transparent, and free

- The only stewardship mechanism specific to GE trees
- Stakeholder developed, global, comprehensive, adaptable, value chain driven
- In English & Portuguese – responsibleuse.org

**Responsible Use:** Biotech Tree Principles

A publication by the Institute of Forest Biotechnology
Everyone wants a safer, faster, responsive, and more efficient regulatory approach

Overhaul Unified Framework (or start from scratch) to:

1. Balance risk of using GE tree w/ risk of not using it or moving too slowly to combat disaster.
2. Incorporate voluntary and adaptive management measures.
3. Address realities of global economy and trade. Trees and pests don’t recognize our political borders.
4. Stop regulating based on process or categories of technologies. It’s a trap. Focus only on what really matters: the end product.
5. Expand public outreach, education, and real participation in making changes. Do it holistically, not just w/ open comments.