GE crops and gene flow
Roundup Ready Wheat and related Problems

Steve Strauss and Carol Mallory-Smith
Oregon State University
Plan

• The problem
• Gene flow concepts
• Two case studies with Oregon focus
  • Roundup Ready (RR) wheat
  • RR creeping bentgrass
• The legal and regulatory context
  • Regulatory loopholes?
  • Gene flow and legal-patent issues
• Summary lessons
Oregon GMO “wheat-gate” shows the risks from gene flow with GE crops, even research

An agreed safe, well studied, extremely rare GMO left over from earlier research nearly crippled Pacific Northwest trade in wheat in 2013, led to lawsuits

Due to fear of...

Adventitious Presence (AP) = Low Level Presence (LLP)

...of unapproved genes in shipped wheat
Global admixture of GM and non-GM crops/food have created immense coexistence problems.

Many costly cases of trade disruption and lawsuits with corn, soy, and rice.

Numerous costly LLP incidents

### LLP incidents: Enduring threats to international trade

<table>
<thead>
<tr>
<th>Commodity</th>
<th>Source</th>
<th>GM Trait</th>
<th>Year</th>
<th>Origin</th>
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<tr>
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<td>GA 21</td>
<td>2007/08</td>
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<td>LLP from asynchronous authorization</td>
<td>LibertyLink, Roundup Ready 2, MON 88017, MIR 604 and others</td>
<td>2008/09</td>
<td>North America</td>
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<tr>
<td>Maize</td>
<td>LLP from asynchronous authorization</td>
<td>Herculex RW Rootworm, MIR 162 and others</td>
<td>2006/07</td>
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<td>LLP from asymmetric authorization</td>
<td>CDC Triffid</td>
<td>2009/10</td>
<td>Canada</td>
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<tr>
<td>Rice</td>
<td>LLP from asymmetric authorization</td>
<td>LLRICE601, LLRICE06 and LLRICE62</td>
<td>2006/07</td>
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</tbody>
</table>

Ruth Rawlings, EU, 2013 -- LLP = low level presence of unauthorized GMO products
LLP cause of major trade disruptions worth >>millions

Arrows show where AP for specific varieties led to decline in trade from USA.
Adventitious presence can affect a very large number of products

Large financial impacts from recalls

The use of derivatives in food products – a case study

Ruth Rawlings, EU, 2013 -- LLP = low level presence of unauthorized GMO products
Numerous cases of AP, large and small, recorded courtesy of Greenpeace & GeneWatch

http://www.gmcontaminationregister.org/
A tough problem for Oregon
Major coexistence struggles due to large seed industry, much non-GMO production, and many exports

Oregon Governor’s GMO Task Force Report - 2014
Large source of anger from organic, GMO-free producers whose markets often impose near zero tolerance.

Special Report: HIGH COSTS, HIGHER STAKES

How organic farmers are being forced to bear the costs (and the risks) of GMO contamination.
A personal issue for me and OSU

GMO ban voted on in Benton County 2015

Fear of admixture with GE-free, organic farms the underlying motivation
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Gene flow = genetic admixture, is ubiquitous in agriculture – with or without GMOs
Many avenues for gene flow — wind, animal and water vectors

- Pollen
- Seed
- Vegetative propagules
- Seed handling
- Volunteer crops
- Adventitious presence
- Compatible relatives
- Weedy or invasive
- Admixture
How to manage this messy system

- Tolerances established in food products for off type varieties, as well as insect parts, mycotoxins, etc
- Growers communicate, often informally, to minimize interference
- Seed purity standards require stricter tolerances, greater care and coordination
- Voluntary seed associations help farmers communicate, and rarely, to mediate conflicts
  - Willamette Seed Association one example
- Balance of farmer right to farm and desire to minimize harm to neighbors
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RR wheat story

- Monsanto developed glyphosate (Roundup) resistant wheat in the late 1990s
- Field tests were conducted in 16 states from 1998 through 2005
- FDA approved a specific event for food and feed in 2004, but USDA never deregulated them
- Monsanto closed the project in 2005 due to anticipated trade problems and probable market loss due to overseas opposition
RR wheat discovered years later, after research ended

• In 2013, an eastern Oregon grower reported that wheat plants in his field that were sprayed with glyphosate did not die.
• In April 2013, plants were sent to OSU Mallory-Smith laboratory for testing.
• The plants tested positive for the specific CP4 gene that confers glyphosate resistance.
• Monsanto and USDA tests confirmed the OSU results.
Important additional details of molecular studies

• Results of Mallory Smith study indicated that there was more than one cultivar
  • It is likely that the seed source may have been a breeding line

• Outcrossing likely occurred because there was a mixture of....
  • Red and white cultivars
  • Hard and soft cultivars
  • Spring and winter cultivars
USDA investigates, markets hold their breadth

- Because of regulated status, USDA-APHIS initiated an investigation into the source of the problem
  - Disrupted Asian markets for several months
- No other cases of admixture found in Pacific Northwest after hundreds of tests
  - Much later some discovered in Montana near to an old test site
  - Not a trade concern given location and rarity
- Results of the USDA investigation released, but causes not discovered
- Markets were restored, some lawsuits settled
- Industry remains interested in developing GE wheat in closer coordination with trading partners
RR creeping bentgrass story

- RR creeping bentgrass was planted in a control area near Madras, OR, for seed production in 2002 before deregulation.
- Control area was established by Oregon Department of Agriculture in response to industry concerns about gene flow.
RR creeping bentgrass disperses

• After the fields were swathed, a wind storm moved panicles with seed out of the fields
  • Very tiny and abundant seeds from ~300 acre field “trial”

• RR creeping bentgrass was not deregulated so all plants needed to be found and removed

• In 2013, RR creeping bentgrass was identified in Kentucky bluegrass fields more than 4 miles from the nearest GE production fields
RR bentgrass found along waterways, drainage ditches
Creeping bentgrass today

- RR creeping bentgrass is still a regulated article
- EIS is still not finished 13 years after plantings
- Control will be difficult to impossible especially on waterways
- Industry continues to be interested in low mowing, RR forms of turfgrasses
- These may escape USDA regulation

Scotts’ GM grass grows free from regulation

Scotts Miracle-Gro is developing a turf grass that has been genetically modified (GM) to grow shorter, thicker and darker green than its conventional counterparts. The enhanced grass from the Marysville, Ohio-based lawn and garden company is yet another novel plant to fall outside the purview of the US Department of Agriculture (USDA), according to documents released in December on the agency’s “Regulated Letters of Inquiry” web page.

Scotts says the grass—a tall fescue variety—will require less mowing and fewer nutrient inputs and is also glyphosate tolerant. The genetic material that conferred these traits in the new grass comes from various undisclosed plants and is integrated using established biolistics technology. In this technique, a gene gun bombards cells with heavy metal particles coated with plasmid DNA fired at high speed. Because this transformation technique requires no genetic material from bacteria, viruses or other organisms considered plant pests, the resulting enhanced plants are not subject to oversight by the USDA. Scotts notified the USDA in April 2013 of its intentions to develop the grass. In January 2014, the federal agency confirmed that the plant was not a regulated article.

Tall fescue is one of at least three GM turf grasses Scotts is developing that doesn’t require USDA oversight. The other two—a variety of St. Augustine grass and a variety of Kentucky bluegrass, both engineered to be shorter, thicker, darker green and glyphosate tolerant—were disclosed to the USDA in January 2012.

A concern that some researchers and growers have raised about Scotts’ tall fescue is that it can cross with non-GM grass species, potentially causing market disruptions for other growers, particularly those who export to countries where GM plants are not permitted. And unlike for grasses that are subject to USDA’s oversight, Scotts doesn’t have to publicly disclose whether or not it is conducting field trials or the genes it is using to confer the traits—something that must be done for regulated GM plants before commercialization. Without knowing what the transgenic material is, “we don’t even know how to test for it,” says Carol Mallory-Smith, a weed scientist at Oregon State University. “It’s a big discussion out here in seed country.”

Scotts has said it will not grow its GM cultivars in Oregon, where much of the non-GM proprietary tall fescue seed is produced. The company also says it will insert into the trait construct of its GM grasses a genetic marker and can provide sequence information to interested parties, such as non-GM grass producers, weed scientists and governments, who want to identify the GM cultivars, says Bob Harriman, vice president of biotech at Scotts. Harriman says the company's Kentucky bluegrass and St. Augustine grass are in field trials, and tall fescue is still in greenhouse development.

Scotts first tested the regulatory system in 2010 when it argued in a letter to the USDA that another variety of Kentucky bluegrass engineered only for glyphosate tolerance was not subject to the agency’s oversight. The agency in July 2011 agreed, making the grass one of the first GM plants to officially slip the agency’s regulatory process (Nat. Biotechnol. 29, 772–773, 2011).

The grass set a precedent (Nat. Biotechnol. 30, 215–217, 2012). Since then, various developers have inquired about at least 20 different biotech plants. In all but three of those cases, the agency has agreed that the plants do not require oversight, according to federal documents posted on USDA of those cases reviewed by Nature Biotechnology. For example, the USDA has said it has no authority to oversee a GM lobolly pine with increased wood density made by Ridgeville, South Carolina–based Arbogen, and a GM soybean engineered for altered flavonoid profiles made by the University of Georgia in Athens.

Emily Waltz Nashville, Tennessee
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Many other GE crops might escape regulation – should they?

Genetically engineered crops that fly under the US regulatory radar

To the Editor:
Recently, the US Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) has categorized as outside the scope of its regulations several genetically engineered (GE) crops that rely on either new approaches or new wrinkles on traditional recombinant DNA techniques in their provenance. Indeed, a survey of recent inquiries to APHIS suggests that the number of entities seeking nonregulated status for their products has been on the increase. Many of these inquiries originate from public institutions or small biotech companies, suggesting that the use of technologies, such as null segregants, novel delivery systems, CRISPR/Cas9, and site-directed nucleases, may be a deliberate strategy for smaller entities to navigate the US GE crop regulatory framework. The fact that the US Coordinated Framework is on the one hand failing to oversee these new product types and on the other overregulating GE crops and technologies with proven track records of safety should be a cause for concern. We conclude that it is time to reevaluate the US regulatory framework for GE crops and build a system that is based on science, with enough flexibility to evolve with accumulating scientific knowledge and technologies and, importantly, that allows the participation of small companies and public sector institutions.

Figure 1 Deregulated and nonregulated status determinations issued by APHIS. Whereas the number of FONSIs (findings of no significant impact; document issued upon successful petition for deregulated status) peaked in the mid-1990s and significantly decreased thereafter, the number of products determined to fall outside of the current regulatory framework has increased only in the past 5 years. Of major interest, 2012 was the first time that the number of nonregulated determinations surpassed the number of FONSIs issued.
Diverse products can avoid regulation.
<table>
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<th>Category</th>
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<th>Transformation method</th>
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<td>12/11/07</td>
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<td>Increased anthocyanin production (intragenic)</td>
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What about genome editing?

Regulatory uncertainty over genome editing

Huw D. Jones

Genome editing opens up opportunities for the precise and rapid alteration of crops to boost yields, protect against pests and diseases and enhance nutrient content. The extent to which applied plant research and crop breeding benefit will depend on how the EU decides to regulate this fledgling technology.

We are at the dawn of a new paradigm in plant breeding. Classical approaches to crop improvement based on hybridization and selection can now be complemented by targeted genome editing that exploits knowledge of specific gene sequences in a systematic way. Unlike conventional genetic modification that results from the insertion of large pieces of exogenous DNA, or maize renders the plants highly resistant to lepidopteron pests; these lepidopteron-resistant crops are grown around the world. However, this technique cannot be used to make small edits to existing genes, and can lead to the random disruption of native genes because the destination of the inserted DNA cannot be dictated.

In contrast to traditional genetic modification, genome editing makes use of one or a few bases at the cut site, resulting in a mutation. Mutations generated in this way are indistinguishable from those that occur naturally and drive evolution, as well as from those induced through the application of chemical mutagens or radiation, as employed in mutation breeding programmes since the 1940s.

Here, I focus on the potential applications and regulation of this simple ‘cut and repair’
New frontier is contract law: “Shrink wrap” agreements

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339158 Rev. 12/06
SEC. THIRAM 2C
Can you be sued for inadvertent GMO contamination of your seed?

- In theory yes – using even a small amount of patented technology could infringe patent
- A major myth among public, and fear among non-GMO producers, that it happens frequently – allowing Monsanto to seize farms and worse!
- Percey Schmeiser case widely told
  - Grew RR Canola in Canada that he did not buy
  - Monsanto sued him
  - But lost in front of Canadian Supreme Court due to extensive amount he grew, and that he knew or should have known what he was doing (using patented materials without a license)
- The key was intention, not accidental/incidental use
What about organic and non-GMO growers? Can they be sued?

- Organic Seed Assn (OSGATA et al.) sued Monsanto to “expressly waive any claim for patent infringement [Monsanto] may ever have against [appellants] and memorialize that waiver by providing a written covenant not to sue.”
- Monsanto has policy on website addressing inadvertent contamination
- US Court of Appeals ruled in favor of Monsanto as no evidence of a lawsuit against innocent contamination was ever found to have been brought by Monsanto
- Monsanto has brought legal action among numerous growers who intentionally saved or sold their seed
Gene flow does not preclude organic certification

- USDA organic standards do not prohibit adventitious presence in an organic product
- Organic producers and some seed industries set the standard for zero tolerance
  - Extremely difficult and unrealistic for co-existence to occur
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Summary message: Gene flow happens

• Inbreeders like wheat, soy as well as outbreeders like maize, canola, trees
• Seed as well as pollen, especially with large scale production, are important sources
  • In some cases vegetative propagules as well
• Zero gene flow essentially impossible beyond boutique or non-flowering research trials
  • This should be recognized at the outset
• But can be serious implications for coexistence, market value of affected crops, trade, and legal liabilities
No easy answers

2014 Task Force Report

Governor’s Task Force on Genetically Engineered Seeds and Agricultural Products
Gene flow: Moving Forward - Research

- Gene flow and GE regulations provide a major impediment to field research in most crops
- Transgenes generally considered “guilty” until proven safe
  - No safe level
- Critical problem with weakly domesticated crops, wild relatives
  - Trees, grasses, and fruits
Gene flow: Moving forward – In practice

• Unrealistic that specialty markets can be protected in all cases
  • Organic still only a few percent of total production, should their interests prevail?
    • In some places where it is a major product?
  • Who has responsibility for mitigation?
  • Who pays compensation and liability?
  • Historically those wanting a more pure, specialty market with a higher price bore the increased production costs

• Right to farm is critical for all parties but definition is difficult depending on time and place

• Setting of legal standards and thresholds a local, national, and international problem
  • Complex biological variation among crops and production systems, and among cultures and laws