



New Breeding Technologies: Regulatory Implications



*San Diego, California
April 16, 2015*

*Scott Thenell
Thenell & Associates LLC
Walnut Creek, CA*

Making News

C&I Comment
 Gary Rodgers
Growing pains

The New York Times
Environmental Review to Delay Two Engineered Crops
 May 10, 2013 • By ANDREW POLLACK
 Genetically engineered crops that could d



TARNISHED PROMISE
 Genetically modified crops generate hype and hatred. A special section of *Nature* cuts through the drama.

SPECIAL ISSUE

nature biotechnology
Agnostic about agriculture
 EDITORIAL

Meeting a global food crisis will require the development of several frontiers for the deployment of new technologies in plant breeding.

It is a common past or present idea that a billion people are hungry, the United Nations estimates. Following people more reliably than a world of 10 billion, those estimates are generally made based on statistical number rather than on actual numbers. The world's population will reach 9 billion in the next 30 years, during which the human race will consume twice as much food as it does today. The global population is projected to rise by 2.5 billion in the next 30 years, with the world's population growing from 7.5 billion in 2013 to 10 billion in 2043. The world's population is projected to rise by 2.5 billion in the next 30 years, with the world's population growing from 7.5 billion in 2013 to 10 billion in 2043. The world's population is projected to rise by 2.5 billion in the next 30 years, with the world's population growing from 7.5 billion in 2013 to 10 billion in 2043.

A NEW BREED
 The next wave of genetically modified crops is making its way to market — and might just ease concerns over 'Frankenfoods'.

When the genetically modified (GM) supercorns...

Making News



Workshop Summary

Examining the Oversight Issues of Plant Targeted Genetic Modification (TagMo)

June 7th, 2013

University of Minnesota

Karen A Korslund, Anders Victor,

A photograph of a field of golden wheat under a blue sky, positioned in the lower right quadrant of the central box.

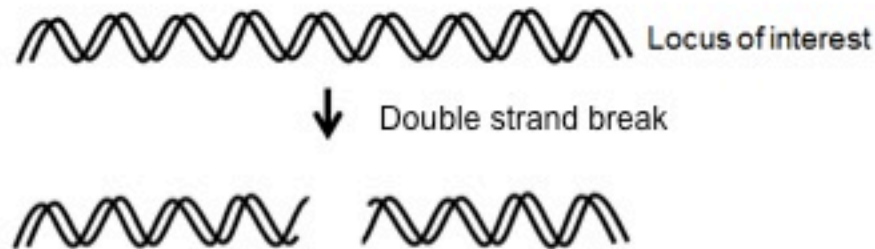
New Breeding Technologies

- What are they
- How are they used
- What are implications for development of analytical methods

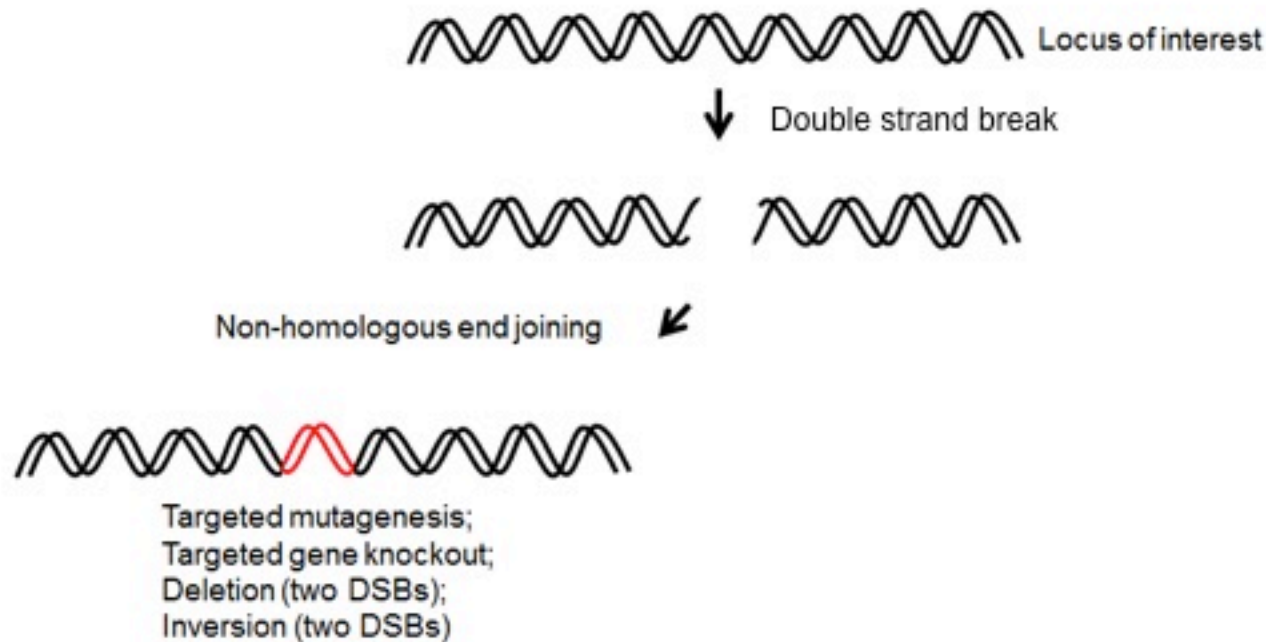
New Breeding Technologies

- Genome editing
 - Site-directed nucleases (ZFN, TALEN, CRISPR, meganucleases)
 - Oligonucleotide directed mutagenesis (ODM)
- Cisgenesis, Intragenesis
- RNA-dependent DNA methylation (RdDM)
- Reverse breeding, Grafting

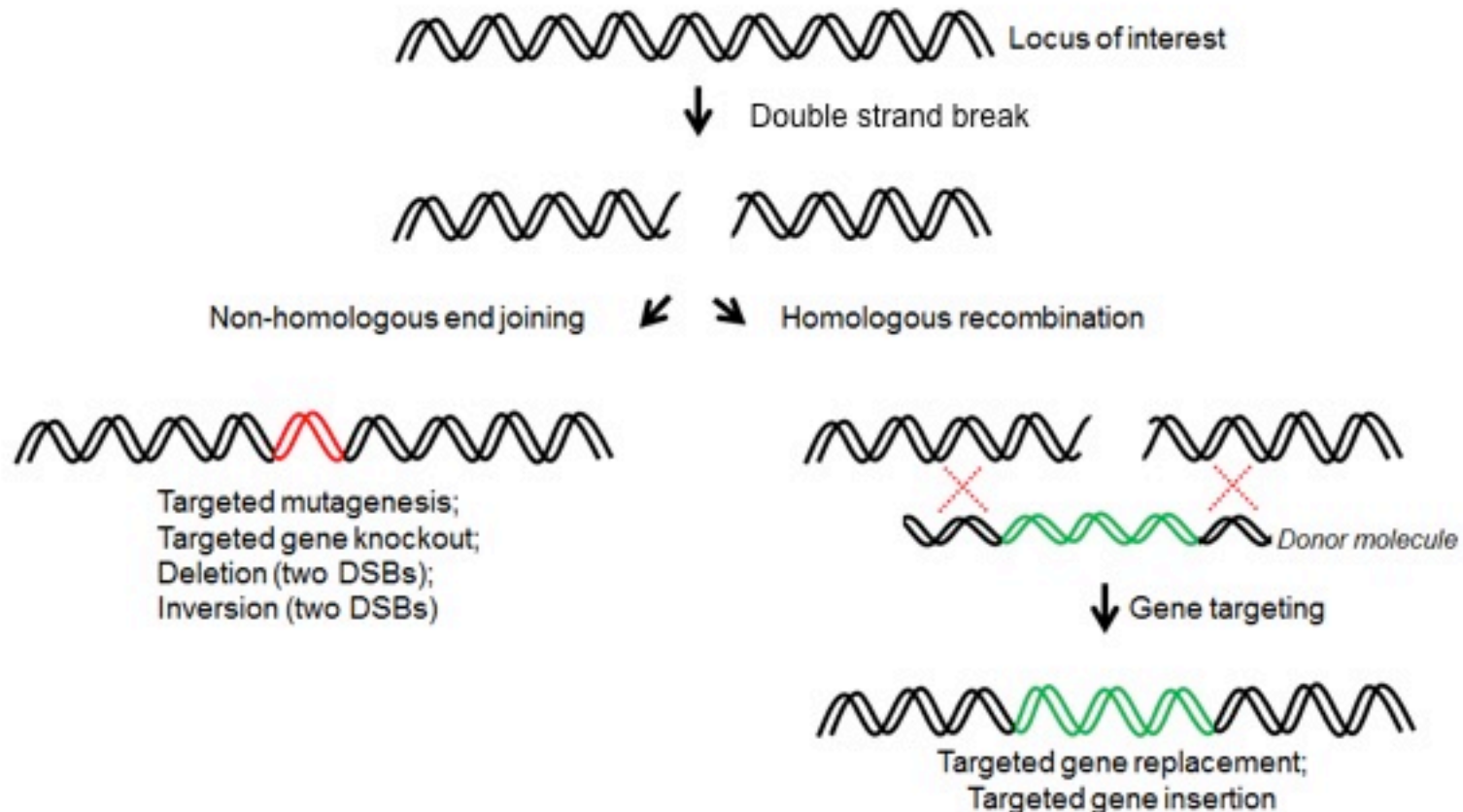
Precise genome modifications are achieved by harnessing DNA double strand break repair pathways



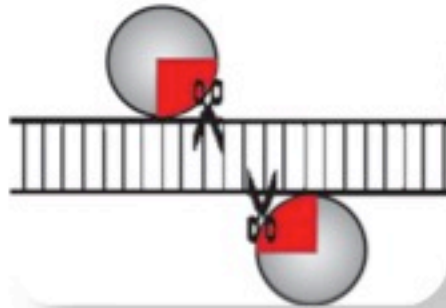
Precise genome modifications are achieved by harnessing DNA double strand break repair pathways



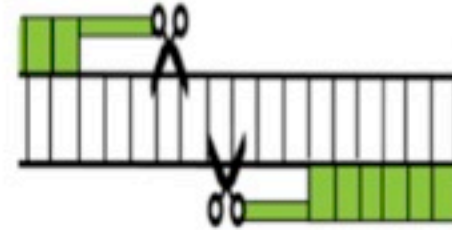
Precise genome modifications are achieved by harnessing DNA double strand break repair pathways



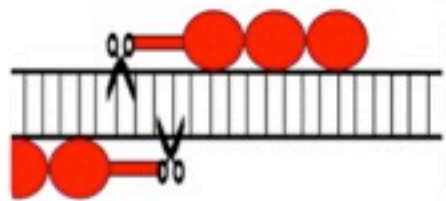
Site Directed Nucleases



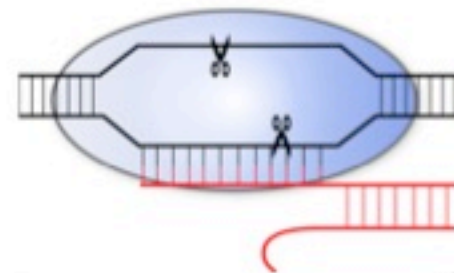
Meganuclease



TALEN



Zinc Finger
Nuclease



CRISPR/Cas

Site Directed Mutagenesis

SDN-1

Targeted mutagenesis or DNA excision

SDN-2

Targeted editing of genome sequence

SDN-3

Targeted gene addition

Gene Knockouts for Crop Improvement

- Remove **toxins** – ricin in castor oil
- Remove **anti-nutrients** – trypsin inhibitors in soybean
- Change **antigenic determinants** – gliadins in wheat; immunogenic epitopes in peanuts
- Knockout gene in phytate biosynthesis to **reduce phosphate** in animal waste
- Improve **nutrient** composition – fatty acid profile in soybean
- Improve **product quality** – reduce cold-induced browning in potato
- Introduce **herbicide tolerance** – imidazolinone resistant rapeseed

Gene Targeting for Complex Traits

- **Carbohydrates** – for food, fuel and industry
- **Fatty acids** – specialty oils for human consumption, fuel and lubricants
- **Proteins** – providing optimal amino acid composition to commodity proteins
- **Secondary metabolites** – pharmaceuticals and specialty chemicals
- **Abiotic stress tolerance** – e.g. drought resistance
- **Biotic stress tolerance** – pest and pathogen resistance

Global Regulatory Environment

- Only certain countries have functional regulatory systems



- Harmonized regulations don't exist
- Variations in pre-market approval data, labeling, post-market surveillance

Europe



- 2007 – Competent Authorities request Commission to establish a Working Group on NPBT
- 2008 - 2012 – *Ad hoc* New Techniques Working Group meets and issues report, but Commission fails to move forward
- 2010 - 2011 – Commission requests a study by EC Joint Research Centre, which issues a final report and international workshop (2012)
- 2011 - 2013 – Commission requests opinion from EFSA on the adequacy of risk assessment guidelines for NBT plants; EFSA opinions on cisgenesis and ZFN-2 and -3

United States



- 2011 – APHIS responds to Scotts-Miracle Grow re: glyphosate tolerant Kentucky bluegrass; publishes opinion on webpage *Am I Regulated?*
- 2012 – APHIS establishes procedure for Regulated Letters of Inquiry increasing transparency, predictability
- 2015 – APHIS rendered over 24 decisions on various organisms (6 by NPBT)

Other Selected Markets



Canada affirms product-based approach (novelty) applies to NPBT (2014)



Science Council of Japan report on Current Trends and Issues of NPBT (2014)



Food Standards Australia New Zealand workshop report on NPBT and food safety (2012)



Environment Agency Austria report of NPBT and Risks Associated with Their Application (2014)



German Federal Food Safety Office decides Cibus' HT rapeseed not GMO; opponents file appeal (2015)

Other Global Instruments

- Cartagena Biosafety Protocol for movement and use of LMO (2003)



- Codex Alimentarius (WHO/FAO) principles for risk analysis of GE foods (2003)



- WTO agreements

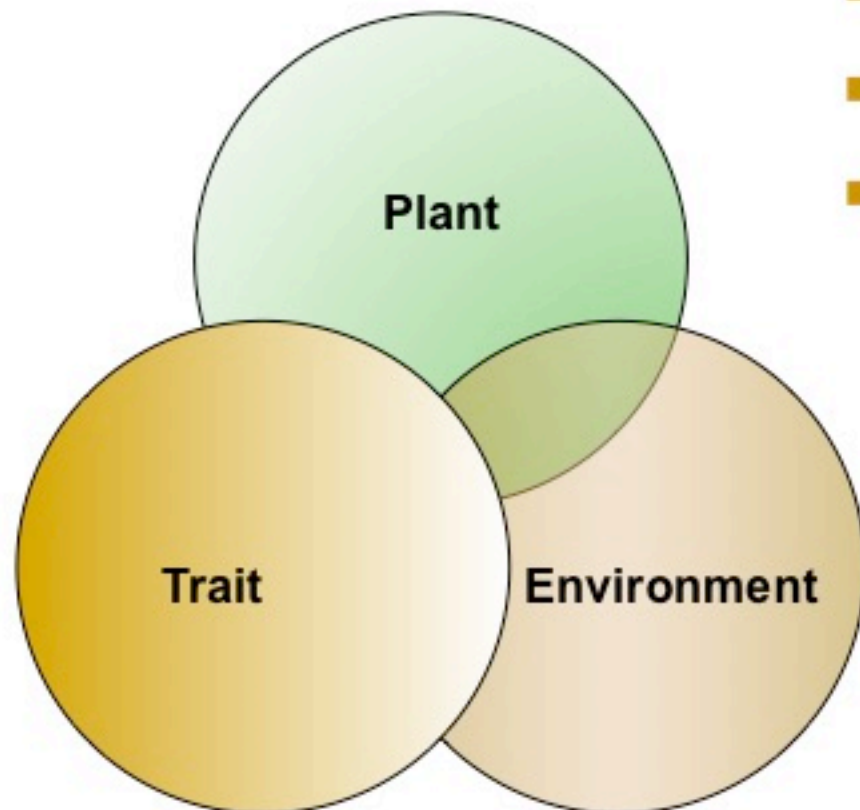


Regulatory Status in Selected Markets

	SDN-1	SDN-2	SDN-3	ODM	Cis / Intra genesis	Reverse Breeding	RdDM
Argentina	Exempt	CBC	<i>Regulated</i>	CBC	<i>Regulated</i>	<i>Exempt</i>	CBC
Australia	Exempt	<i>Regulated, CBC</i>	<i>Regulated</i>	<i>Regulated, CBC</i>	<i>Regulated, CBC</i>	<i>Exempt</i>	<i>Regulated</i>
Brazil	<i>Exempt</i>	<i>Regulated, CBC</i>	<i>Regulated</i>	<i>Exempt</i>	<i>Regulated, CBC</i>	<i>Exempt</i>	<i>Regulated</i>
Canada	<i>Regulated, if PNT</i>	<i>Regulated, if PNT</i>	<i>Regulated, if PNT</i>	<i>Regulated, if PNT</i>	<i>Regulated, if PNT</i>	<i>Exempt</i>	<i>Regulated, if PNT</i>
China	<i>Exempt, CBC</i>	<i>Regulated, CBC</i>	<i>Regulated, CBC</i>	<i>Exempt, CBC</i>	<i>Regulated, CBC</i>	<i>Exempt, CBC</i>	<i>Exempt, CBC</i>
European Union	<i>Exempt, Various MS</i>	<i>Exempt</i>	<i>Regulated</i>	<i>Exempt, Various MS</i>	<i>Regulated, Various MS</i>	<i>Exempt</i>	<i>Exempt</i>
Japan	<i>Exempt</i>		<i>Regulated</i>	<i>Exempt</i>	<i>Regulated</i>	<i>Exempt</i>	<i>Exempt, CBC</i>
New Zealand	Exempt *	<i>Regulated, CBC</i>	<i>Regulated</i>	<i>Exempt, CBC</i>	<i>Regulated</i>		
South Africa	<i>Exempt</i>		<i>Regulated</i>		<i>Exempt</i>		
United States	Exempt, CBC	Exempt, CBC	<i>Regulated, CBC</i>	Exempt	<i>Regulated, CBC</i>	<i>Exempt</i>	<i>Exempt</i>

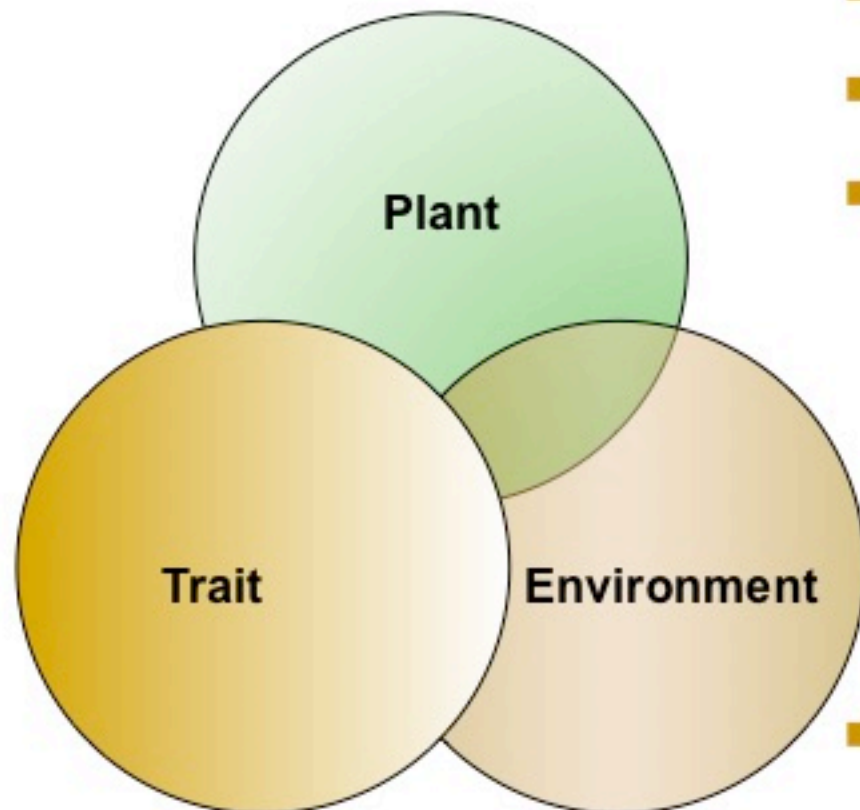
Italics connotes expected status absent published decisions
 * decision overturned by High Court

Risk Assessment Paradigms



- Comparative assessment
- Conducted case-by-case
- Characteristics of plant, introduced trait, receiving environment, and their interactions

Risk Assessment Paradigms



- Comparative assessment
- Conducted case-by-case
- Characteristics of plant, introduced trait, receiving environment, and their interactions
- Paradigm is robust and broadly applicable

Analytical Methods

- Modern technology can detect nearly all genetic alterations
- But, not all genetic alterations can be identified (distinguished from naturally occurring)
 - SDN-1, SDN-2, ODM, RdDM
- Comparative risk assessments still require analytical methods for safety
 - Composition, toxicity, allergenicity
- Traceability, intellectual property are challenging

Summary

- Tools for targeted genome modification are powerful and rapidly being deployed
- Targeted genome modification can provide solutions to critical challenges in agriculture
- Regulation of NPBT is complex, involving both process and product criteria
- Risk assessment paradigms are robust and widely applicable
- One should be pragmatic and not regulate what one cannot enforce



New Breeding Technologies: Regulatory Implications



Scott Thenell
Thenell & Associates LLC
Walnut Creek, CA 94597
[*scott@sthenell.com*](mailto:scott@sthenell.com)
[*abtrnetwork.com*](http://abtrnetwork.com)