Ag-Biotechnology:
Start-up Challenges and Opportunities

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Scott Thenell
Thenell & Associates LLC
Walnut Creek, CA

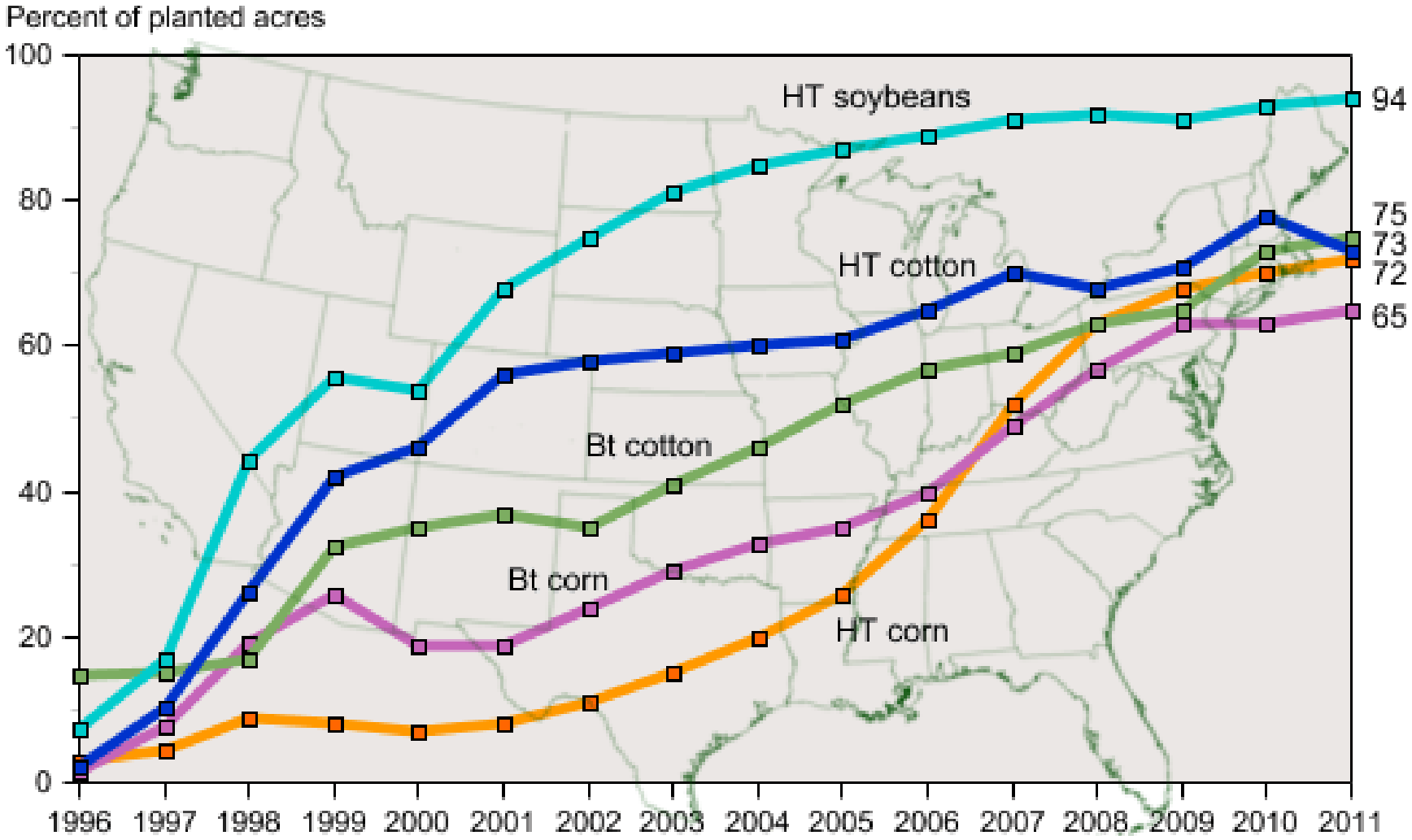
Topics

- Crop biotechnology overview
- Regulatory environment and external challenges
- Product development process
- Points to consider

US Crop Biotechnology Overview

- Since 1987, over 20,000 regulated field trials have been conducted of biotechnology-derived plants in the U.S.
  - Over 6,300 with herbicide-tolerant (“HT”) traits
  - Over 4,700 with insect-resistant (“IR”) traits
  - Over 10,000 with various agronomic and other traits
- 87 biotech plants have been cleared for commercialization (incl. 29 IR traits, 36 HT traits).
- Most biotech crops on the market today are either insect resistant (IR/Bt), herbicide tolerant (HT), or a combination of these two traits (“stacked”).

US Crop Biotechnology Overview



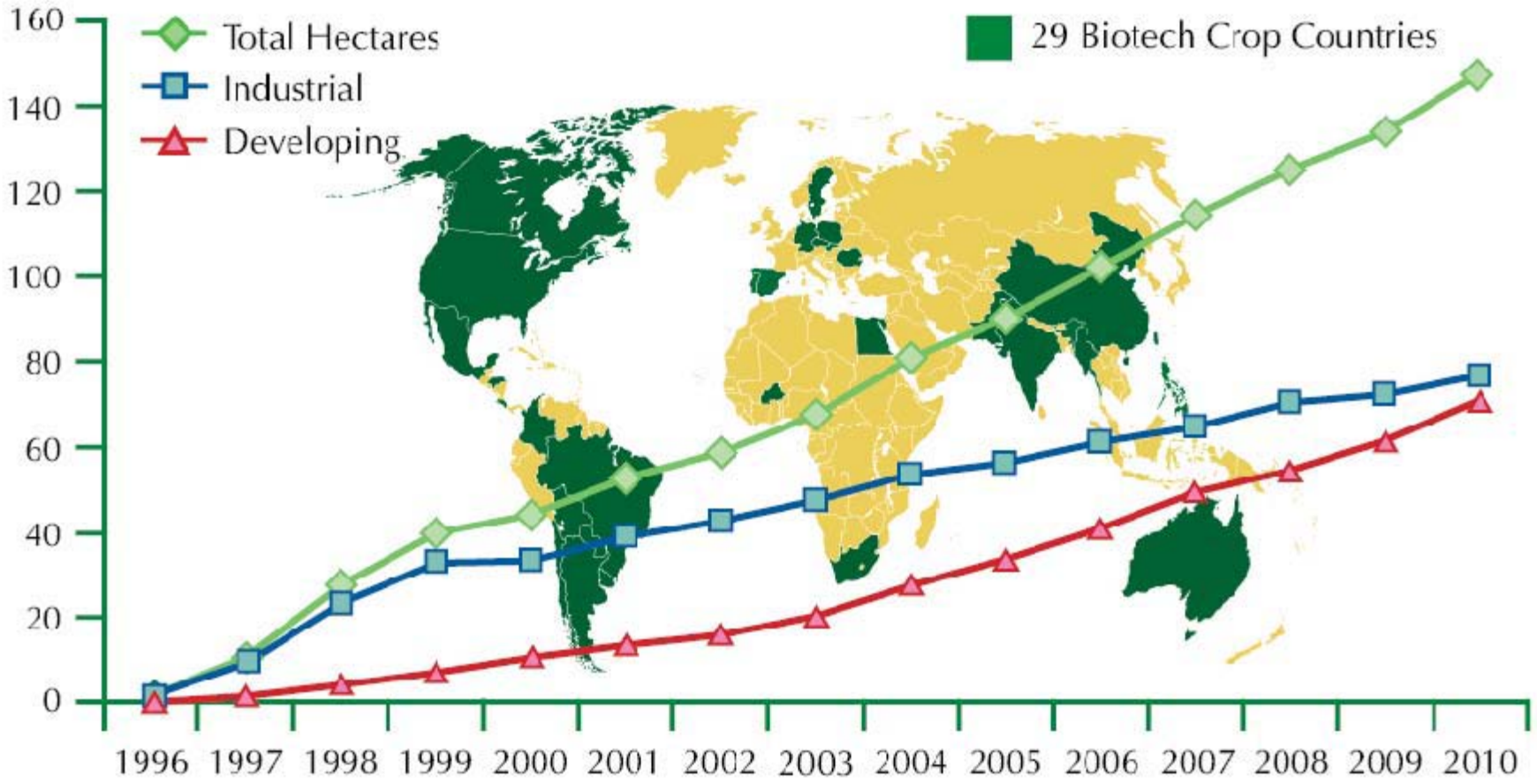
From USDA-ERS, 2011

Global Crop Biotechnology Overview

- Since 1992, 24 countries have approved or deregulated 144 unique crop and trait combinations.
  - Crops are mainly corn, cotton, canola and soybean
  - Traits are mainly HT and IR, and stacks
  - Traits also include product quality, virus resistance, and agronomic properties

From GM Crop Database, CERA , 2010

Global Crop Biotechnology Overview



From C. James, ISAAA , 2010

Global Crop Biotechnology Overview

Top 29 countries planting biotech crops in 2010

- 17 countries grow 100,000 acres or more

1.	United States	11.	Bolivia	21.	Portugal
2.	Brazil	12.	Australia	22.	Czech Republic
3.	Argentina	13.	Philippines	23.	Poland
4.	India	14.	Myanmar	24.	Egypt
5.	Canada	15.	Burkina Faso	25.	Slovakia
6.	China	16.	Spain	26.	Costa Rica
7.	Paraguay	17.	Mexico	27.	Romania
8.	Pakistan	18.	Colombia	28.	Sweden
9.	South Africa	19.	Chile	29.	Germany
10.	Uruguay	20.	Honduras		

From C. James, ISAAA , 2010

Global Crop Biotechnology Overview

Total economic gains from planting of biotech crops from 1996 – 2009 are estimated at $65 billion

- Increased yield/acre (reduced land use)
- Reduced production costs (increased environmental benefit)
  - Reduced insecticide use
  - No or low-tillage of soil (reduced erosion)
  - Reduced fossil fuel use
- Over reliance on glyphosate in some regions has contributed to weed resistance

From Brookes and Barfoot, 2011

Global Regulatory Environment

- Only certain countries have functional regulatory systems

- Harmonized regulations don’t exist
- Variation exist in pre-market approval requirements, labeling, post-market surveillance

Global Regulatory Environment

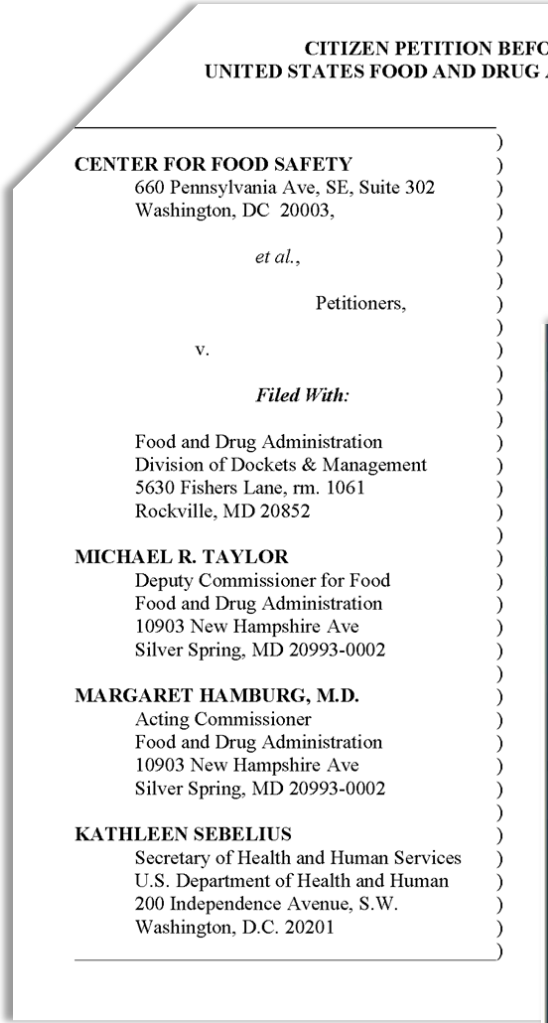
- Cartagena Protocol on Biosafety established minimum requirements for transboundary movement and use of Living Modified Organisms (2003).
  - Precautionary principal
  - Advanced informed consent
  - Liability and redress provisions
  - Particularly important in Less Developed Countries
  - Adopted by 161 countries, but not Australia, Canada, USA

Global Regulatory Environment

- Codex Alimentarius (WHO/FAO) developed principles for risk analysis of genetically engineered foods (2003)
  - Internationally recognized
  - Consistent with US standards, Cartagena Protocol

- WTO agreements have been invoked in trade disputes between members with varying success
  - US/Canada/Argentina vs. EU

External Challenges



CITIZEN PETITION BEFORE THE
UNITED STATES FOOD AND DRUG ADMINISTRATIO

CENTER FOR FOOD SAFETY
660 Pennsylvania Ave, SE, Suite 302
Washington, DC 20003,

et al.,

Petitioners,

v.

Filed With:

Food and Drug Administration
Division of Dockets & Management
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

MICHAEL R. TAYLOR
Deputy Commissioner for Food
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

MARGARET HAMBURG, M.D.
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

KATHLEEN SEBELIUS
Secretary of Health and Human Services
U.S. Department of Health and Human
200 Independence Avenue, S.W.
Washington, D.C. 20201

- CFS coalition petitions FDA to require GE food labeling
- California ballot initiative on labeling slated for 2012

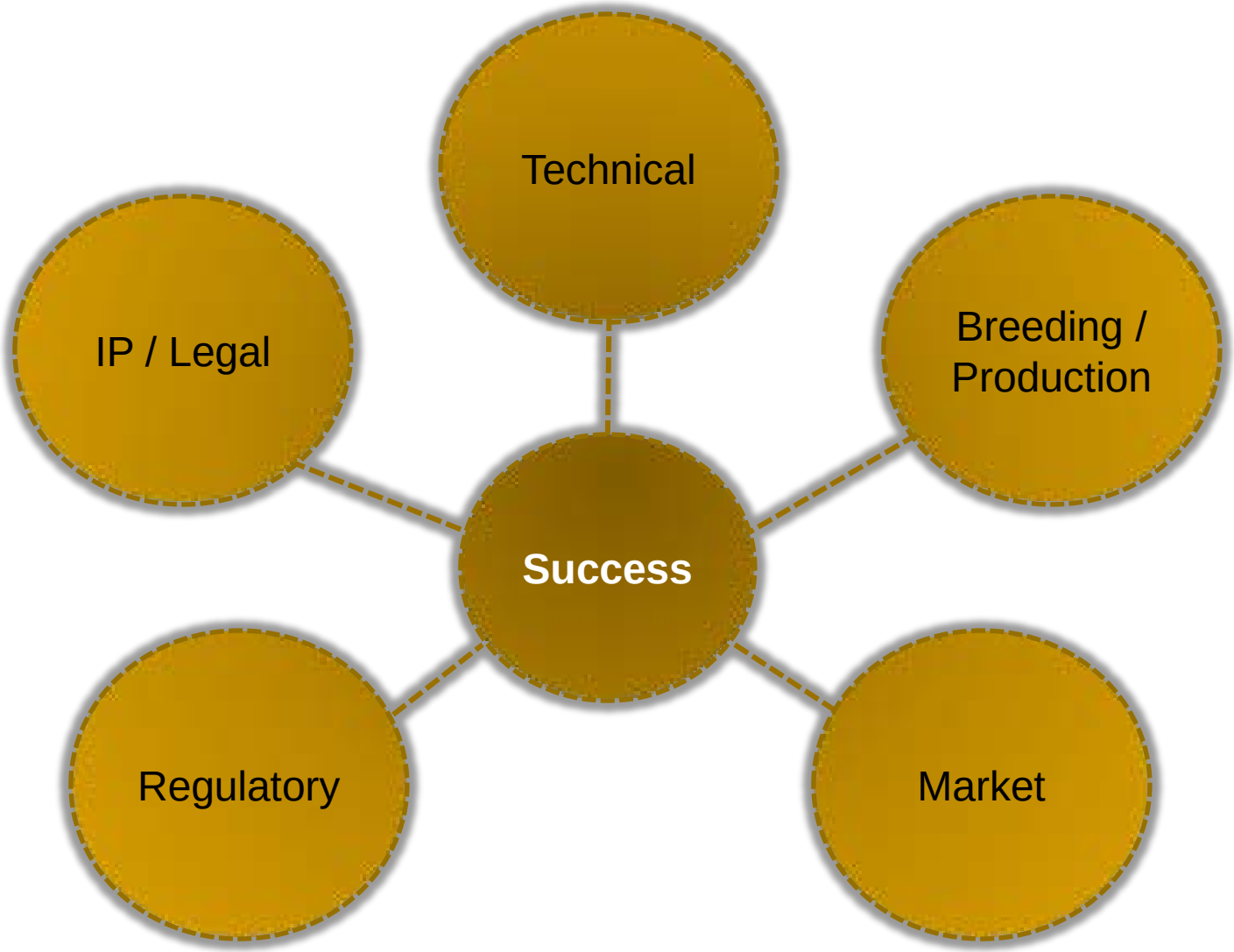
Current Situation

- Crop biotechnology is pervasively regulated.
  - Environmental and human / animal food safety
- Event-based regulation is the norm; further upward pressure on costs to de-regulate new varieties.
- Specialty food crops still largely absent due to market acceptance issues and regulatory costs.
- Food crops engineered for lower inputs (water, nitrogen) gaining importance.
- Non-food energy crops engineered to increase fitness and biomass present new environmental issues.

Current Situation

- Small companies creating new traits, but multinational companies still dominate commercial markets.
- Foreign innovators contribute half of new biotech plant varieties by 2015, challenging US dominance.

Product Development



From D. McElroy, NBT 22, 2004

Product Development

	Discovery	Proof of Concept	Early Development	Advanced Development	Pre-launch
Key Activities	High-throughput screening Model crop testing FTO review	Gene optimization Crop transformation	Trait development Pre-regulatory data Commercial transformations	Trait integration Field testing Regulatory data generation	Regulatory submissions Seed bulk-up Pre-marketing
Duration	2 – 4 years	1 – 2 years	1 – 2 years	1 – 2 years	1 – 3 years
Success	<10%	25%	50%	75%	90%
Candidates	10,000's	1,000's	10's	< 5	1

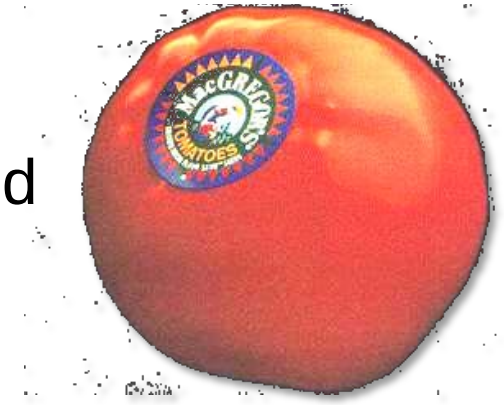
From Monsanto Company, 2009

Regulatory Activities

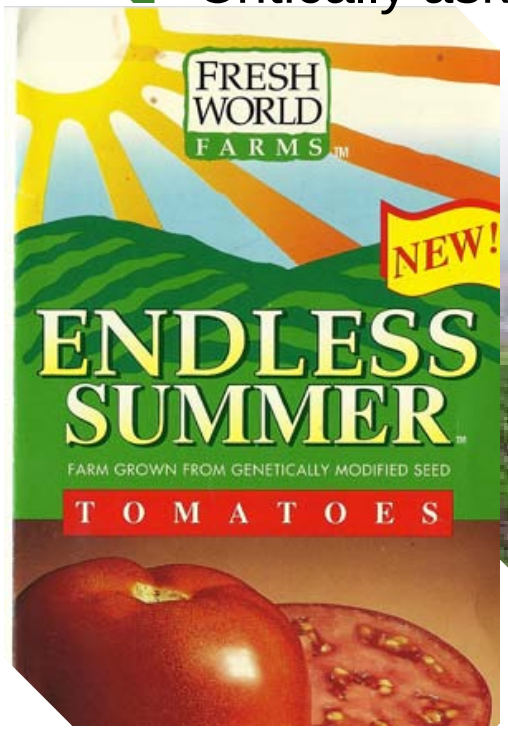
Key Activities				
Crop biology	AA homology	Protein safety assessment	Molecular characterization	Manage regulatory submissions
Target genes	Analytical tools, reagents	Gene expression analysis	Compositional assessment	Acquire approvals: cultivation, imports
Ecologic impacts	Protein production, characterization		Agronomic studies	
Gene flow analysis	Target / export market analysis		NTO studies	
Stewardship plan			Animal perf. studies	
			Environ. fate studies	
			Toxicology	
Projected Costs				
$170 – 1,100K	$767 – 3,485K	$365 – 1,953K	$2,712 – 9,005K	$590 – 2,415K

From Kalaitzandonakes et al., NBT 25, 2007

Points to Consider

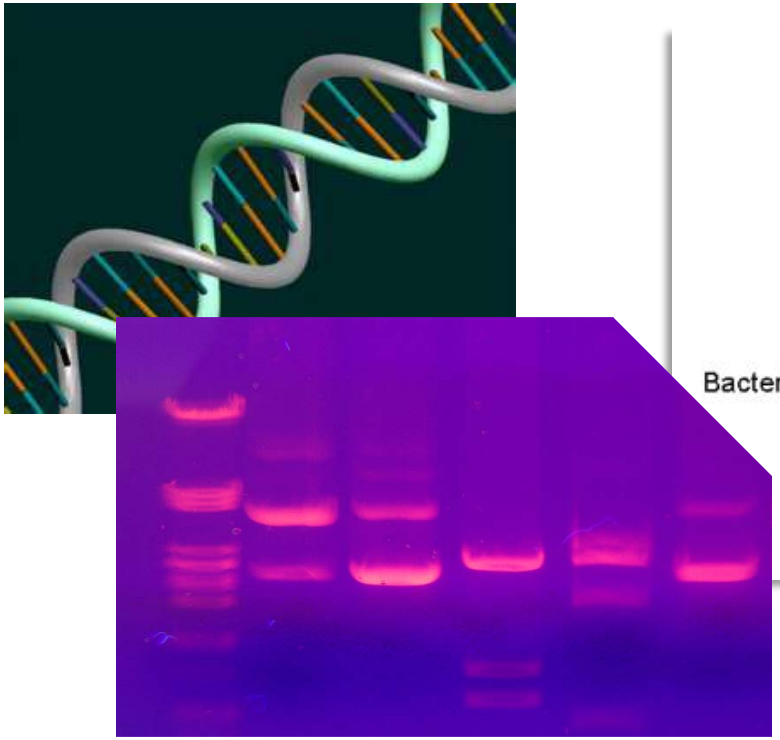


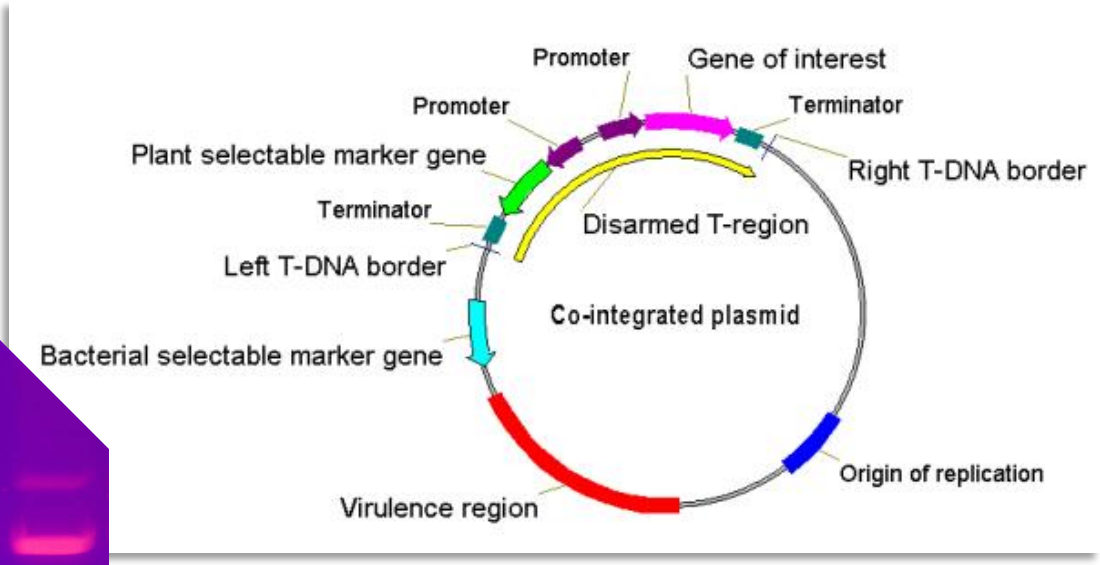
- Product design must address market need efficiently and effectively
  - *Market pull* succeeds over *technology push*
  - Critically ask… *Why this? Why here? Why now?*
  - Map your stakeholders to gauge market acceptance and vulnerabilities



Points to Consider

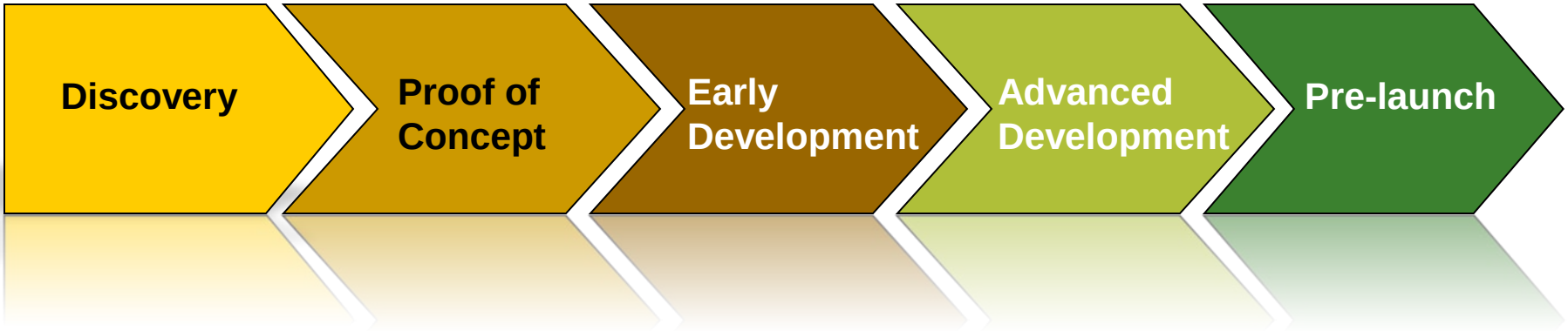
- Incorporate regulatory criteria into product design.
  - Gene source, selection method, construct design





Points to Consider

- Make regulatory review a condition of product advancement



- Shortcutting development stages can be costly.
  - Choosing a transformation event of poor construct design or an exceptionally complex event can increase regulatory costs

Points to Consider

- Establish internal QA/QC procedures and recordkeeping to aid regulatory compliance.
- Ensure access to regulatory data and validation technologies as part of your trait in-licensing activities.

Points to Consider

EXCELLENCE THROUGH STEWARDSHIP®

Advancing Best Practices in Agricultural Biotechnology

- Implement stewardship practices to ensure plant product integrity throughout the product lifecycle

Final Thoughts…

- Exciting opportunities exist for products that meet critical needs.
- Regulatory input can help achieve successful product development.
- Product stewardship is important part of global regulatory compliance and mitigating business risks.

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Start-up Challenges and Opportunities

Scott Thenell
Thenell & Associates LLC
Walnut Creek, CA 94597
scott@sthenell.com
http://abtrnetwork.com