Getting to Yes – How to Achieve Pre-Market Approval

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To learn more, visit www.abtrnetwork.com
“Abandon all hope, ye who enter here”

Dante’s Inferno

Not the objective

Don’t know where to start

Too complicated

Too costly

Intellectual property

Product liability / stewardship concerns

No commercial partnership

No mechanism in public sector
“It’s not complicated, if you plan well…”

- Regulatory environment and other challenges
- Product development process
- Points to consider
Global GM Crop Status

From Clive James, 2012
Global GM Crop Approvals

Since 1992, 33 countries have approved 325 unique crop–trait combinations.

- Crops mainly corn, cotton, canola and soybean
- Traits mainly HT, IR, and stacks
- Traits also include product quality, disease resistance, and agronomic properties

From GM Approval Database, ISAAA, 2013
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
Other Global Instruments


- WTO agreements
US Coordinated Framework

[Logos of USDA, FDA, and EPA]
Recent Headlines

**March Against Monsanto**

5/25, 2 p.m. EST, Everywhere

**The New York Times**

Supreme Court Supports Monsanto in Seed-Replication Case

**The New York Times**

Environmental Review to Delay Two Engineered Crops

May 10, 2013 - By ANDREW POLLACK

Genetically engineered crops that could sharply increase the market for Monsanto products have been delayed by a federal environmental review.

**TIME**

Grocery Chains Won’t Sell Genetically Modified Fish

Feb 26, 2013 - By ALEXANDRA GIFFER

Call them “frankenfish,” but don’t look for genetically engineered salmon at Trader Joe’s or Whole Foods.

Several major grocery chains, including Trader Joe’s, Aldi, Whole Foods, regional stores like March Supermarkets and PCC Natural Markets, as well as some organic supermarket chains such as Rainbow Market and Good ‘N Natural, say they will not sell GM salmon.
Labeling

CITIZEN PETITION BEFORE THE
UNITED STATES FOOD AND DRUG ADMINISTRATION

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

Thenell & Associates LLC
Product Development

- Technical
- Breeding / Production
- Market
- Regulatory
- IP / Legal

From D. McElroy, NBT 22, 2004
Product Development

**Key Activities**

- **Discovery**
  - High-throughput screening
  - Model crop testing
  - FTO review

- **Proof of Concept**
  - Gene optimization
  - Crop transformation

- **Early Development**
  - Trait development
  - Pre-regulatory data
  - Commercial transformations

- **Advanced Development**
  - Trait integration
  - Field testing
  - Regulatory data generation

- **Pre-launch**
  - Regulatory submissions
  - Seed bulk-up
  - Pre-marketing

**Duration**

- Discovery: 2 – 4 years
- Proof of Concept: 1 – 2 years
- Early Development: 1 – 2 years
- Advanced Development: 1 – 2 years
- Pre-launch: 1 – 3 years

**Success**

- Discovery: <10%
- Proof of Concept: 25%
- Early Development: 50%
- Advanced Development: 75%
- Pre-launch: 90%

**Candidates**

- Discovery: 10,000’s
- Proof of Concept: 1,000’s
- Early Development: 10’s
- Advanced Development: < 5
- Pre-launch: 1

From Monsanto Company, 2009
Regulatory Activities

**Key Activities**
- Crop biology
- Target genes
- Ecologic impacts
- Gene flow analysis
- Stewardship plan
- AA homology
- Analytical tools, reagents
- Protein production, characterization
- Target / export market analysis
- Protein safety assessment
- Gene expression analysis
- Molecular characterization
- Compositional assessment
- Agronomic studies
- NTO studies
- Animal perf. studies
- Environ. fate studies
- Toxicology
- Manage regulatory submissions
- Acquire approvals: cultivation, imports

**Projected Costs**
- Discovery: $170 – 1,100K
- Proof of Concept: $767 – 3,485K
- Early Development: $365 – 1,953K
- Advanced Development: $2,712 – 9,005K
- Pre-launch: $590 – 2,415K

From Kalaitzandonakes et al., NBT 25, 2007
Product Design

- Product design must address market needs efficiently and effectively
Regulatory Guidance in Product Design

- Gene source and sequence
- Construct design
- Bioinformatic analysis
- Selection method
Consultation with Regulators

- Novel phenotype or technique can raise new issues
- Incorporate guidance into data acquisition plan
Analytical Tools and Reagents

- Complete vector sequence
- Antibodies and ELISA
- qRT-PCR
- Southerns
- Tail-PCR

- Method validation
  - LOD in test article matrix and conditions
Good Laboratory Practice

- Contract lab, field studies
- Molecular characterization
- Other specialized analyses
Event Selection / Advancement

- Regulatory criteria
  - Absence of vector backbone, single copy, single integration
  - Expected ORFs, expression patterns
  - Agronomics
Publications of laboratory, field efficacy can be powerful.
Stewardship practices ensure product integrity throughout its lifecycle.
Shortcuts Lead to Costly Mistakes

- Poor construct design
- Insufficient tools and reagents
- Inadvertent mixing of events through poor stewardship
- Advancing complex events from proof-of-concept project
- Asking discovery scientist to perform regulatory science
- Incomplete, poor quality data

= Missed deadlines and increased costs
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