Ensuring Food and Feed Safety: U.S. Food Law and FDA’s Biotechnology Consultation Process

Robert I. Merker, Ph.D.
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration
Department of Health and Human Services
Overview

- Regulatory Framework
- Consultation Procedures
- Safety Assessment
- Experience to date
- Conclusions
Authority for Regulating Genetically Engineered Crops

The Legal Basis
It’s the Law!
Regulation of Genetically Engineered Plants Under the Coordinated Framework

- **USDA**: Safe for agriculture and the environment
- **FDA**: Safe for use in food and feed
- **EPA**: Safe for use as pesticide

Timeline:
- 1986
- 1992
- NOW
FDA’s Legal Framework for Foods From New Plant Varieties
U. S. Food Law

The Purveyors Responsibility

What FDA Does
The legal requirements

<table>
<thead>
<tr>
<th>As Safe as Conventional</th>
<th>• Food Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Truthful &amp; Not Misleading</td>
<td>• Food Labeling</td>
</tr>
<tr>
<td>Is Premarket Review Required?</td>
<td>• Food Additive</td>
</tr>
</tbody>
</table>

- 1986
- 1992
- NOW
FDA’s Authority: FD&C Act

Adulteration

Unsafe Pesticide Chemical

Unsafe Food Additive

Contains poisonous/deleterious substance

Post Market Authority

Pre-market Authority

1986

1992

GRAS Substance

FDA’s decision

• Safe according to food safety experts

Food Additive

FDA’s decision

Contains poisonous/deleterious substance
What would be a food additive in a genetically engineered plant?

<table>
<thead>
<tr>
<th>New Protein or Product</th>
<th>Safety Information not Publicly Available or Widely Accepted</th>
</tr>
</thead>
</table>

STOP

Requires FDA Review before marketing
Other legal/regulatory issues: Labeling

Truthful | Misleading
As safe as other foods

Decision Trees

Consult Early and Often

1986

1992

NOW

1992 Policy
Evaluation by Two FDA Centers for Different Uses

CFSAN
Human Food Safety

CVM
Safety for Animal Feed
Consultation Processes

- How we interact
- Early and Often
- Early Food Safety Assessments
Consultation Procedures Under 1992 Policy

On The Internet
http://www.fda.gov/bioconprocguidance
# What are the Issues?

<table>
<thead>
<tr>
<th>Safety</th>
<th>Potential for Toxicity?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Potential for Allergenicity?</td>
</tr>
<tr>
<td></td>
<td>Anti-Nutrients?</td>
</tr>
<tr>
<td></td>
<td>Bioavailability?</td>
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</table>

<table>
<thead>
<tr>
<th>Regulatory</th>
<th>Unapproved Food Additive or GRAS?</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Meaningful difference?</td>
</tr>
</tbody>
</table>
Consultation Procedures

Tell us your story... about the new plant variety and why it is safe for food use..
Consultation Procedures: FDA’s role

Recognizing Variation
Without Genetic Engineering

Receiving the submission

Evaluating the submission

Asking for clarification

Developing Documents

Sending a Letter
Early Food Safety Evaluations (NPCs)

Guidance issued June 2006 entitled:
Recommendations for the Early Food Safety Evaluation of New Non-pesticidal Proteins Produced by New Plant Varieties Intended for Food Use

Is it toxic?  Y  N
Is it allergenic?  Y  N
Safe for Field Testing

On the Internet
http://www.fda.gov/npcguidance
http://www.fda.gov/npcinventory
Safety Assessment

- The data and information needed to conduct a safety assessment
Safety Assessment

New Substances
- Identity
- Source
- Weight of Evidence

Effects in the Plant
- Composition
- Agronomic

Agronomic & Quality
- Eliminate some lines

Unintended Effects
- New ORFs
- Fusion Protein
Safety Assessment

- Genetic Analysis
  - Stability
  - Unintended effects

- Chemical & Nutritional Analyses
  - Dietary impact
  - Levels of toxicants

- Allergenicity
  - Toxicity
Safety assessment resources

**FDA**

**Codex Alimentarius**
- Guidelines on Foods derived from Modern Biotechnology

**OECD**
- Molecular Characterization of Plants Derived from Modern Biotechnology
- Consensus documents on Safety of Novel Foods and Feeds: Plants
How do we conclude that a Genetically Engineered plant is as safe as other varieties for food/feed use?

Case-by-case approach

Comparative Approach

Focus on the New Substance
Protein Safety Assessment

Protein Safety: Potential for Toxicity

Protein Safety: Potential for Allergenicity
The Molecular Assessment

- Incorporation into Genome
- No Vector Backbone
- New Proteins from ORFs
- Copy Number & Stability
Experience to date

- What FDA’s Consultation Program Has Seen
What we’ve evaluated: The Crops

- Alfalfa
- Canola
- Cantaloupe
- Corn
- Cotton
- Creeping bentgrass
- Flax
- Papaya
- Plum
- Potato
- Squash
- Sugar beet
- Soybean
- Tomato
- Wheat

Pie chart showing the distribution of crops with corn being the largest segment, followed by cotton and canola.
## What we’ve evaluated: the traits (90+ to date)

<table>
<thead>
<tr>
<th>Trait</th>
<th>Crops</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herbicide tolerance</td>
<td>alfalfa, canola, corn, cotton, soybean, sugar beet, creeping bentgrass, flax, rice</td>
</tr>
<tr>
<td>Virus Resistance*</td>
<td>Squash, plum, papaya</td>
</tr>
<tr>
<td>Insect Resistance*</td>
<td>corn, cotton, potato, soybean, tomato</td>
</tr>
<tr>
<td>Altered composition oils</td>
<td>Soybean, canola</td>
</tr>
<tr>
<td>Male Sterility</td>
<td>Corn, canola, radicchio</td>
</tr>
<tr>
<td>Delayed ripening</td>
<td>Tomato, cantaloupe</td>
</tr>
<tr>
<td>Altered composition</td>
<td>Corn (increased lysine)</td>
</tr>
<tr>
<td>Altered composition composition</td>
<td>Canola (reduced phytate)</td>
</tr>
<tr>
<td>Agronomic changes</td>
<td>Corn</td>
</tr>
</tbody>
</table>
Types of traits

- **RNAi**
  - Uses “hairpin” structures to lower expression of proteins

- **Plant Incorporated Protectants (Pesticidal Proteins)**
  - EPA assesses food/feed safety (pesticide/inerts, FDA looks at stability and nutrition

- **Non-pesticidal proteins**
  - Well known enzymes
  - Well understood functions

- **EPA + FDA authority**
Risk Communication
Transparency

- Internet
- Freedom of Information Act (FOIA)
  - Formal process to request publicly releasable information from the US Federal government
- Direct Communication
  - Correspondence with consumers, industry, other government agencies, NGOs
  - Notice of public comment periods, citizen petitions

On the Internet
http://www.fda.gov/bioconinventario
FDA Internet Resources

- [www.fda.gov](http://www.fda.gov)  
  - Main webpage for all things FDA
- [www.fda.gov/GEPlantFoods](http://www.fda.gov/GEPlantFoods)  
  - Main webpage for Biotech Consultation Program
- [www.fda.gov/npcguidance](http://www.fda.gov/npcguidance)  
  - Guidance on New Protein Consultations
- [www.fda.gov/bioconinventory](http://www.fda.gov/bioconinventory)  
  - Inventory of Completed Submissions  
  - Final Consultations and New Protein Consultations
# Conclusions and The Future

<table>
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<tr>
<th>As Safe As</th>
<th>Foods from GE plants as safe as their traditionally bred counterparts</th>
</tr>
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<tbody>
<tr>
<td>Engagement</td>
<td>Developers have engaged with FDA prior to marketing</td>
</tr>
<tr>
<td>Communication</td>
<td>FDA talks to its sister government agencies and other agencies worldwide</td>
</tr>
<tr>
<td>Evolution</td>
<td>As the technology matures, expect new traits.</td>
</tr>
</tbody>
</table>
Thank You!

Questions?
- Contact Robert Merker
- robert.merker@fda.hhs.gov
- Available by telephone during business hours

On The Internet
http://www.fda.gov/GEPlantFoods