GM Foods:
Safety and Regulation

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Biotechnology: Agricultural, Food, Nat. Resource Issues
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Overview

- Background on Food Biotechnology
- Genetically Modified (GM) Foods: Consumer attitudes, potential benefits
- How are GM foods regulated?
- Food safety perspectives: GM foods vs. traditional
- Labeling issues for GM foods
Background: Food Biotechnology

• Goals
  – Propagate / selectively breed plants and animals to excel in some desirable property or characteristic
  – Develop plants and animals which:
    • Grow faster
    • Produce more, increased fertility
    • Better quality
    • Use resources more efficiently
    • Resistance to disease, environmental stress
Food Biotechnology

• Traditional examples
  – Classical plant breeding
  – Rennet enzyme (cheesemaking)
  – Yogurt “starter bacteria” cultures
  – Enology (wine making)
  – Brewing science (malted barley)
  – Breadcrumbing
Food Biotechnology: Traditional Breeding vs. GM

• **Traditional breeding**
  - Exchanging all genetic material from two related plants
    - Hybridization
    - In-vitro fertilization
    - Tissue culture

• **Genetic modification (GM)**
  - Moving one or two genes selectively across a species barrier
    - Recombinant DNA (rDNA) technology
    - Cell fusion
    - Microencapsulation
Food Biotechnology

- Biotechnology is not new; farmers have crossbred and hybridized plants for centuries.
- Modern genetic modification technologies provide new tools to target specific food characteristics for enhancement.
- Recombinant rDNA biotechnology offers the potential to make the process more precise.
Recent examples (transgenic engineering)

- Milk from cows receiving Bovine Somatotropin (growth hormone, rGBH)
- Chymosin enzyme (cheesemaking)
- Calgene’s FlavrSavr™ tomatoes
- Papaya (resistance to ringspot virus)
- High oleic / low linolenic soybean oil, sunflower oil
- Insecticide-resistant corn
  - Bt (*Bacillus thuringeinsis*) corn Monsanto
  - Cry9C (insecticidal protein) *Starlink* corn Aventis
- Herbicide-tolerant soybeans (Round-up ready)
# Existing Genetically Engineered Food Crops

**Primary Benefit: Agricultural Production**

<table>
<thead>
<tr>
<th>Food</th>
<th>Engineered Traits</th>
<th>Gene Source</th>
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</thead>
<tbody>
<tr>
<td>Canola</td>
<td>herbicide resistance</td>
<td>bacteria, virus</td>
</tr>
<tr>
<td>Chicory</td>
<td>facilitates hybridization</td>
<td>bacteria</td>
</tr>
<tr>
<td>Corn</td>
<td>insect resistance</td>
<td>bacteria (Bt)</td>
</tr>
<tr>
<td>Papaya</td>
<td>ringspot virus resistance</td>
<td>bacteria, virus</td>
</tr>
<tr>
<td>Potato</td>
<td>insect resistance</td>
<td>bacteria (Bt), virus</td>
</tr>
<tr>
<td>Soybean</td>
<td>herbicide resistance</td>
<td>bacteria, virus</td>
</tr>
<tr>
<td>Squash</td>
<td>virus resistance</td>
<td>bacteria, virus</td>
</tr>
<tr>
<td>Sugarbeet</td>
<td>virus resistance</td>
<td>bacteria, virus</td>
</tr>
</tbody>
</table>
Genetically-Modified Foods

Approximately 70% of foods in U.S. supermarkets are produced by genetic modification (not just fresh fruits and vegetables in Produce section)

- Soybean
  - Lecithin (emulsifier used in chocolate)
  - Oil (mayonnaise, pourable salad dressings, margarine)
  - Meat substitutes (e.g. “bacon” bits, breakfast sausage analogs)
- Corn
  - High fructose corn syrup (soft drinks, candy, fruit juice cocktails)
  - Corn starch (puddings, mixes, gravies, cold cereals)
- Chymosin enzyme
  - Cheese manufacture
- Aspartame (artificial sweetener – GMO bacteria)
  - Soft drinks, candy, fruit spreads, fruit in yogurt
Future Consumer Benefits: GM Foods

- Fifty varieties of GMO-enhanced crops have been approved in the United States (2000)
- Food industry is the recipient of university and life science company research on new food crops and ingredients:
  - Increased nutrients (proteins, vitamins, minerals) and “healthy” fatty acid profiles (lower levels of saturated fats) in fruits, vegetables, grains
  - Ripening / freshness extension for fruits and vegetables; better taste
  - Vitamin A / β-carotene enhancement (Golden rice)
  - Modified potatoes with more solids content, permitting less oil absorption during manufacture of French fries and potato chips
  - Vitamin C-enhanced strawberries, sweet potatoes
  - Vitamin E-enhanced canola oil
  - Allergen-free peanuts and soybeans
  - Higher antioxidant levels in tomatoes
  - Caffeine-free coffee beans
- Once consumers are able to enjoy the direct benefits of these new GMO foods, debate may diminish about the risks and benefits of this technology.
Regulation of GM Foods

What is the regulatory process for developing and marketing new GM foods?
U.S. Food Regulations

• The Federal Food, Drug, and Cosmetic Act gives the FDA jurisdiction to regulate that foods are safe, wholesome, and fairly represented / marketed to the public

• The regulation of food safety centers around the legal aspects of “adulteration”:
  – Poisonous or deleterious substances  *mercury in canned fish*
  – Avoidable contaminants  *plant stems in spices*
  – Filthy, putrid, or decomposed substances  *mold, insect parts*
  – Containers  *plastic packaging residues*
  – Unfit for food  *tough and rubbery clams*
  – Sanitation / Good manufacturing practices  *time, temperature, pH monitoring for preventing microbial contamination of acidified foods*

• Foods that are adulterated, misbranded, or sold without required pre-market approval are subject to a recall (removal from commerce) by FDA
The GM Food Development Process

1. **Trait Discovery**
   - Early-stage risk analysis

2. **Product Development**
   - Advanced risk analysis

3. **Safety Assessment**
   - Regulatory approval

4. **Commercialization**

   USDA
   EPA
   FDA
The GM Regulatory Triangle

**USDA - APHIS**  
U.S. Department of Agriculture,  
Animal & Plant Health Inspection Service  

**EPA**  
Environmental Protection Agency  
[http://epa.gov](http://epa.gov)

**FDA**  
Food & Drug Administration  
[http://vm.cfsan.fda.gov](http://vm.cfsan.fda.gov)
GM Food Approval Process

1. Biosafety Review Committee
   * Scientific expert panel (follows 1994 NIH “Health Guidelines for Research Involving Recombinant DNA Molecules”)

2. USDA/APHIS
   * Protects agriculture against invasive GM species which may promote infestation by plant pests or diseases
     * Reviews greenhouse facilities for standards & inspections
     * Authorizes field trials
     * Authorizes transport for field trials
   * When ready for commercialization, applicants request “determination of non-regulated status”

* Opportunity for public input
GM Food Approval Process

3. EPA

Regulates plants and microbiological organisms which produce pesticidal substances (insecticides, herbicides)
* - Reviews effects on environment (toxicity, residuals)
* - Approves experimental use permits
* - Authorizes product registration

4. FDA

Ensures the safety of food and feed products, including those derived from new plant varieties
- Voluntary pre-market consultation
- Regulates new foods (genetic sources and functions)
- Monitors food composition, altered nutritional profiles
- Assesses potential food toxicants, allergens

* Opportunity for public input
USDA Food Safety
Assessment of GM Foods

USDA-APHIS:
– Early field testing of genetically engineered plants under plant test statutes
– Detailed environmental assessments required before issuing permits; scientific peer-review
  • Genetic material is stably integrated
  • Plant modification does not contain genetic material derived from an animal or human pathogen
  • Function of genetic material is known, and its expression does not result in plant disease
  • Introduced genetic material does not produce an infectious entity, or encode substances likely to be toxic to nontarget organisms likely to feed on the plant
  • New GM sequences do not pose significant risk for creating a new plant virus
– In 1993, the permit application system was replaced by a notification system
FDA Food Safety Initiative

Coordination

Surveillance

Inspections

Risk Assessment

Research

Education
FDA Safety Assessment of GM Foods

Focuses on the following areas:

- Safety and nutritional value of newly-introduced proteins
- Identity, composition, and nutritional value of modified carbohydrates, fats, or oils
- Concentration and bioavailability of important nutrients for which a food crop is consumed
- The potential of food allergens to be transferred from one food source to another
- Toxins characteristic of host and donor plants
MOTHER GOOSE & GRIMM

I bought some new pet food at the health store.

It's supposed to be really good for you.

It's made of tofu and oat bran.

And I bet in ten years some FDA report will call it "a silent killer."
“Big-Eight” Food Allergens

- Peanuts and peanut products
- Shellfish (shrimp, crab, lobster, crayfish)
- Fish (finfish)
- Eggs and egg products
- Milk and dairy products (cheese, yogurt, cultured)
- Tree nuts (almonds, walnuts, pecans, Brazil nuts, hazelnuts)
- Soybeans and foods made with soy protein (tofu)
- Cereals containing gluten (wheat, rye, barley, oats)

Allergenic proteins tend to be resistant to digestion, and stable to food processing, particularly heat processing

“Substantial Equivalence”

• Compares foods (food ingredients) from genetically-modified crops to their conventional counterparts
  – Origin of genes
  – Agronomic parameters
  – Composition (key nutrients / anti-nutrients)
  – Consumption

“Relative safety”
Possible Outcomes

- Substantially equivalent to conventional counterpart:
  - no further testing

- Substantially equivalent to conventional counterpart except for introduced trait(s):
  - focus assessment on trait(s) / gene product(s)

- Not substantially equivalent to accepted food or food component:
  - combined nutritional / toxicological assessment
# Compositional Analyses to Establish Substantial Equivalence (Corn Example)

Evaluate Key:
- Nutrients
- Vitamins
- Minerals
- Anti-nutrients
- Toxicants
- Allergens
- Others

List depends on crop

<table>
<thead>
<tr>
<th>Grain</th>
<th>Forage</th>
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<tbody>
<tr>
<td>Protein</td>
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<tr>
<td>Fat</td>
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<td>Fiber</td>
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<tr>
<td>Starch</td>
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<tr>
<td>Amino acid composition</td>
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<tr>
<td>Fatty acid composition</td>
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<tr>
<td>Ash</td>
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<tr>
<td>Sugars</td>
<td></td>
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<tr>
<td>Calcium</td>
<td></td>
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<tr>
<td>Phosphorous</td>
<td></td>
</tr>
</tbody>
</table>
Safety Assessment Approach

Gene / Protein

- Gene(s)
  - Source(s)
  - Molecular characterization
  - Insert / copy number / gene integrity

- Protein(s)
  - History of safe consumption
  - Function / specificity / mode-of-action
  - Levels
  - Toxicology / allergenicity
    - Amino Acid homology
    - Digestibility
    - Acute oral toxicity
    - Clinical

Food / Feed Safety

Substantial Equivalence

- Crop Characteristics
  - Morphology
  - Yield

- Food / Feed Composition
  - Proximate analysis
  - Key nutrients
  - Key anti-nutrients
  - Feed performance studies
    - Wholesomeness

Courtesy: Steve Taylor, Univ. of Nebraska
Food Safety

The fundamental question:

– Are foods produced via genetic engineering safe and wholesome to eat?
What, if anything, are you most concerned about when it comes to food safety? *(1,000 respondents)*

- **Food handling / prep**
- **Disease / contamination**
- **Ingredients**
- **Packaging**
- **Chemicals / pesticides**
- **Other**
- **Nothing**
- **Genetically engineered**
- **Don’t know**

Source: International Food Information Council, 2002
FDA Perspective: GM Foods

- (1992) After lengthy debate, industry researchers and government regulators concluded that biotech crops and food ingredients do not compositionally differ in any substantial way from ordinary food products.
- Therefore, they should be regulated by the same standards applied to non-GM crops and foods.
Food Industry Perspective: GM Foods

• Responds to consumer demand
• Mostly remains neutral on the use of biotechnology to enhance whole and processed foods
• Supports “substantial equivalence” scientific viewpoint
• In some cases, industry has rejected GM food ingredients in response to perceived consumer opinion to protect market share (Frito-Lay, Beechnut, Ben & Jerry’s)
Food Professional and Trade Perspective: GM Foods

Grocery Manufacturer’s of America, Institute of Food Technologists, Center for Science in the Public Interest, American Medical Association

• Based on the perspective of industry researchers, government regulators, and independent scientists who have studied the safety and applications of modern biotechnology

• Overwhelming verdict is that GM technology is safe, and offers a multitude of food benefits:
  – Lower cost
  – Better tasting
  – Healthier, more nutritious
  – Abundant food supply to meet global population needs
Scientific Endorsements:

GM Foods

• Pro
  Institute of Food Technologists
  American Dietetic Association
  American Medical Association
  The National Research Council
  Center for Science in the Public Interest
  U.S. National Academy of Sciences
  World Health Organization
  European Research Commission
  International Food Information Council

Trade Associations
  Grocery Manufacturers of America
  National Food Processors Association
Scientific Opponents: GM Foods

- Con
  
  Union of Concerned Scientists
  Foundation on Economic Trends
  Center for Food Safety

Clubs & Trade Associations
- Organic Trade Association
- Sierra Club
- Greenpeace
GM Foods: Critics Perspective

- Genetic engineers cannot control with precision where genetic material will be inserted into a host plant, and how it will interact with other genes
- Scientists do not fully understand the impact that genetic changes can have on nutrition, toxicity, and other food properties
- Genetic manipulations may permit wider spread of allergenic proteins in foods
- Unintended ecological consequences as super-weeds, oversize fish, rapidly-evolving plant viruses
Food Industry Response: GM Foods

• No other foods in history have been tested and observed as diligently as those developed from modern biotechnology.

• For more than two decades before approval for the consumer market, GM crops and their derivatives were laboratory- and field-tested to ensure safety for human and animal consumption.
Global Regulatory Mechanisms

• Regulations differ greatly in scale and implementation:
  – Industrialized countries (US, Japan) – extremely restrictive; 71% of transgenic crop field trials from 1986-1999 were in US, Canada
  – Developing countries – virtually non-existent

• New European Union regulations of GM foods took effect on April 18, 2004. Requires labeling if > 1% GM

• Dealing with such disparities will become increasingly important with growth in international trade, and need for intellectual protection
Food Safety and GM Corn

- Monsanto first develops *Bt* corn with Cry1Ab protein as insect toxin
- Aventis pursues development of StarLink corn with Cry9C protein, an alternative insect toxin
- Allergen testing showed that Cry9C was unlikely to be an allergen, since it does not share amino acid, protein structure similarities with known allergens
- Unlike other Cry proteins, Cry9C is not readily digestible in simulated gastric conditions, and is stable at 90°C
- In 1998, EPA registration required that StarLink corn was to be restricted solely to animal feed uses
Food Safety and GM Corn

- The existing U.S. grain storage and distribution system was incapable of adequate grain segregation, identity preservation.
- The EPA affirms that allergenicity risks are “extremely low”
- In Fall, 2000 Kraft recalled 2.5 million boxes of Taco Bell™ taco shells made using corn contaminated with StarLink corn. Total industry recall costs: “several $10 million”.
- Aventis has asked the EPA to reconsider Cry9C’s allergenicity in light of new data it offered, and to rule it safe for human consumption.
- In July 2001, EPA ruled that there was inadequate information to establish a tolerance (legal residue limit) for use in human food products. Aventis voluntarily withdrew Starlink.
Brazil Nut Saga

• Pioneer Hi-Bred International
  – Tried to correct the methionine deficiency in soybeans
  – Brazil nuts rich in methionine; Brazil nut storage protein expressed in transgenic soybean successfully increases methionine content
  – But, was the Brazil nut storage protein an allergen?
Brazil Nut Saga

- Testing of Brazil nut storage protein
  (Univ. of Nebraska / Univ. of Wisconsin)
  - Recruited 9 subjects with Brazil nut allergies
  - Of the 9, 8 had antibodies that recognized the Brazil nut storage protein as an allergen
  - Three subjects were skin-prick tested with the Brazil nut storage protein
  - The protein elicited an allergic response in all 3
Brazil Nut Saga

• Pioneer Hi-Bred International “did the right thing” and discontinued product development, notified FDA

• Still, however, negative publicity resulted for Pioneer
  – Jeremy Rifkin/ USA Today editorial
Food Labeling

– Should GM foods be labeled?
GM Labeling

FDA only requires labeling of rDNA technology-derived foods that differ significantly in composition, nutritional value, or safety from their conventional counterparts.
Labeling Debate: Pro

• Arguments for Labeling
  – Consumers’ right to know to make purchasing decisions
  – Consumer polls support labeling
  – Failure to label may be interpreted as trying to cover-up negative attributes of these foods
  – FDA requires labeling of irradiated food and food ingredients, which it claims is compositionally similar to non-irradiated
  – Without mandatory labeling, “reverse” labeling (made without GMO’S) is inevitable

Consumers Union, Campaign to Label Genetically Engineered Foods, Greenpeace
National Organic Program Definition

• Allows “organic foods” label to be used for foods that apply traditional breeding processes to produce genetic modification

• Excludes recombinant DNA techniques and methods to achieve gene deletion, gene doubling, introduction of a foreign gene, and changing of gene positions

http://www.ams.usda.gov/nop
Labeling Debate: Con

• Arguments against Labeling
  – Current government regulations are sensible.
  – Genetically engineered foods are compositionally the same as their conventional counterparts. There’s nothing to label.
  – Mandatory labeling is over-regulation. Consumers have other choices (e.g., organic foods) and the marketplace is working.
  – There are no marketed gene-altered foods containing allergens.
  – Mandatory labels would wrongfully imply that safety or nutritional value has been compromised in GM foods, and could lead to consumer confusion about them.
  – Requiring new labeling would raise food costs.

Analytical Testing

• In general, rDNA is not detectable in highly heat-treated foods, hydrolyzed plant proteins, starch derivatives, and refined oils from GM food crops

• Two common analytical methods for GM foods:
  – Polymerase Chain Reaction (PCR) method: Detects genetically modified DNA sequences. Qualitative test, $250 – $600 per sample
  – Enzyme Linked Immunosorbent Assay (ELISA) test: Measures levels of proteins expressed by inserted DNA sequences. Quantitative test, $75 – $100 per sample

• Both require trained staff and specialized equipment.

• Sample turnaround times for results are typically 3-5 days

Because tests are extremely sensitive, risk of cross-contamination can result in false-positives
Conclusions

• The GM food issue is highly complex
• Researchers agree that there are legitimate and valid arguments on both sides of the GM issue
• Additional scientific discourse is essential to find common ground that would allow new technology to be developed and adopted
• Such actions will be in the best interests of society
Conclusions

• Plant biotechnology products must meet stringent performance standards during development

• Continuous regulatory oversight occurs throughout development and the full authorization process

• Candidate genes / proteins are assessed prior to transformation

• All products are thoroughly assessed for food, feed, and environmental safety prior to regulatory approval
Conclusions

• Food/feed safety is based on substantial equivalence and safety of expressed proteins
• Proteins currently produced in plants have a history of safe use