

# Food and Feed from GE plants: U.S. Approach to Safety Assessment

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Office of Food Additive Safety

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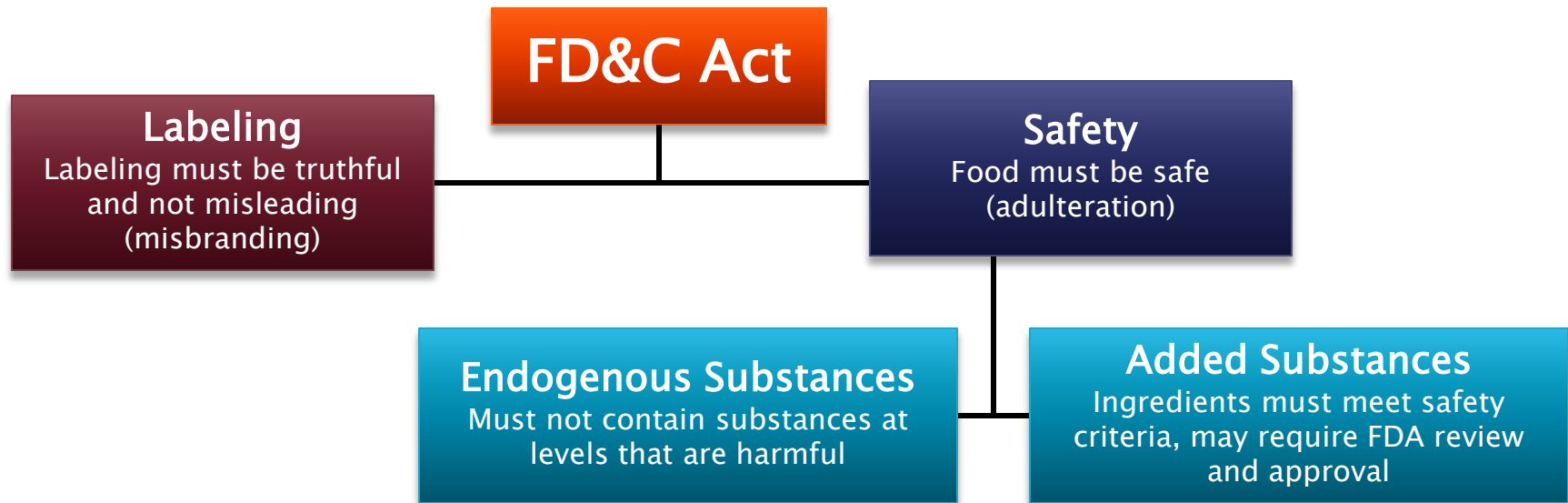
**U.S. Food and Drug Administration**  
Protecting and Promoting *Your* Health

# Overview



- ▶ FDA's Approach to Food and Feed Safety Assessment
  - Elements of the safety evaluation of food and feed from GE crops
  - Hypothetical case: GE banana
  - Evaluations to-date

# Federal Food Drug & Cosmetic Act (FD&C Act)



**1992 Statement of Policy:  
Foods Derived from New Plant Varieties**

- elements of the safety evaluation

# Elements of the Safety Evaluation

## Basic Information

### Endogenous Substances

Must not contain substances at levels that are harmful

### Added Substances

Ingredients must meet safety criteria, may require FDA review and approval

- ▶ Information about the crop species
- ▶ Intended use
- ▶ Molecular characterization
- ▶ Trait stability



# Elements of the Safety Evaluation

## Basic Information

### Endogenous Substances

Must not contain substances at levels that are harmful

### Added Substances

Ingredients must meet safety criteria, may require FDA review and approval

## ▶ Compositional assessment:

- Key nutrients
- Anti-nutrients
- Toxicants
- Allergens

## ▶ Comparative approach

- Relative to other commonly consumed varieties

## ▶ If there are differences, do they raise safety issues?



# Elements of the Safety Evaluation

## Basic Information

### Endogenous Substances

Must not contain substances at levels that are harmful

### Added Substances

Ingredients must meet safety criteria, may require FDA review and approval

## ► Toxicity assessment

- Is the source organism safely consumed?
- Is the source organism known to have toxic proteins?
- Is the new protein similar to known toxic proteins?
- Level of exposure? Fate? Further toxicological studies?



# Elements of the Safety Evaluation

## Basic Information

### Endogenous Substances

Must not contain substances at levels that are harmful

### Added Substances

Ingredients must meet safety criteria, may require FDA review and approval

## ▶ Allergenicity assessment

- Is the source organism known to be allergenic?
- Is the new protein similar to known allergens?
- Digestibility and heat stability?
- Human serum testing?

## ▶ New metabolic pathways?





# Hypothetical case: GE banana

## Basic Information

- What do we know about bananas?
- How are bananas used?
- What is the genetic change? Is it stable?

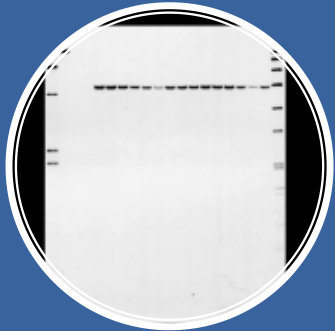


**INGREDIENTS:** WATER (75%), **SUGARS (12%)** (GLUCOSE (48%), FRUCTOSE (40%), SUCROSE (2%), MALTOSE (<1%)), STARCH (5%), FIBRE E460 (3%), **AMINO ACIDS (<1%)** (GLUTAMIC ACID (19%), ASPARTIC ACID (16%), HISTIDINE (11%), LEUCINE (7%), LYSINE (5%), PHENYLALANINE (4%), ARGININE (4%), VALINE (4%), ALANINE (4%), SERINE (4%), GLYCINE (3%), THREONINE (3%), ISOLEUCINE (3%), PROLINE (3%), TRYPTOPHAN (1%), CYSTINE (1%), TYROSINE (1%), METHIONINE (1%)), **FATTY ACIDS (1%)** (PALMITIC ACID (30%), OMEGA-6 FATTY ACID: LINOLEIC ACID (14%), OMEGA-3 FATTY ACID: LINOLENIC ACID (8%), OLEIC ACID (7%), PALMITOLEIC ACID (3%), STEARIC ACID (2%), LAURIC ACID (1%), MYRISTIC ACID (1%), CAPRIC ACID (<1%)), ASH (<1%), PHYTOSTEROLS, E515, OXALIC ACID, E300, E306 (TOCOPHEROL), PHYLLOQUINONE, THIAMIN, **COLOURS** (YELLOW-ORANGE E101 (RIBOFLAVIN), YELLOW-BROWN E160a), **FLAVOURS** (3-METHYLBUT-1-YL ETHANOATE, 2-METHYLBUTYL ETHANOATE, 2-METHYLPROPAN-1-OL, 3-METHYLBUTYL-1-OL, 2-HYDROXY-3-METHYLETHYL BUTANOATE, 3-METHYLBUTANAL, ETHYL HEXANOATE, ETHYL BUTANOATE, PENTYL ACETATE), 1510, NATURAL RIPENING AGENT (ETHENE GAS).

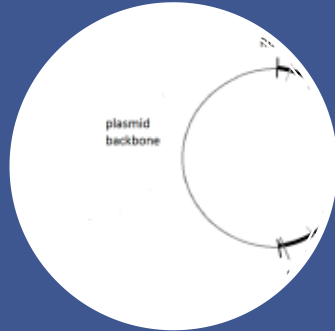
<http://jameskennedymonash.wordpress.com/2013/12/12/ingredients-of-an-all-natural-banana>



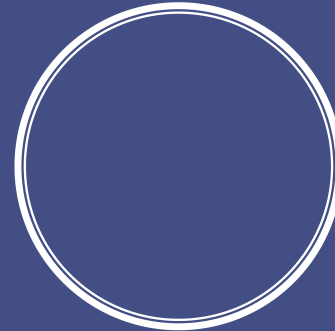
# Molecular Assessment



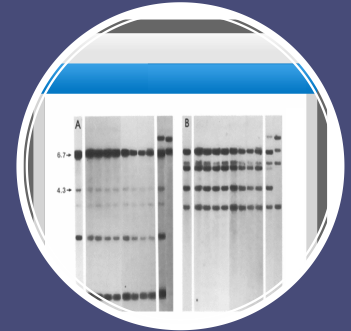
Incorporation  
into Genome?



Vector  
Backbone?



New Proteins  
from ORFs?



Copy Number  
& Stability?



# Compositional Assessment

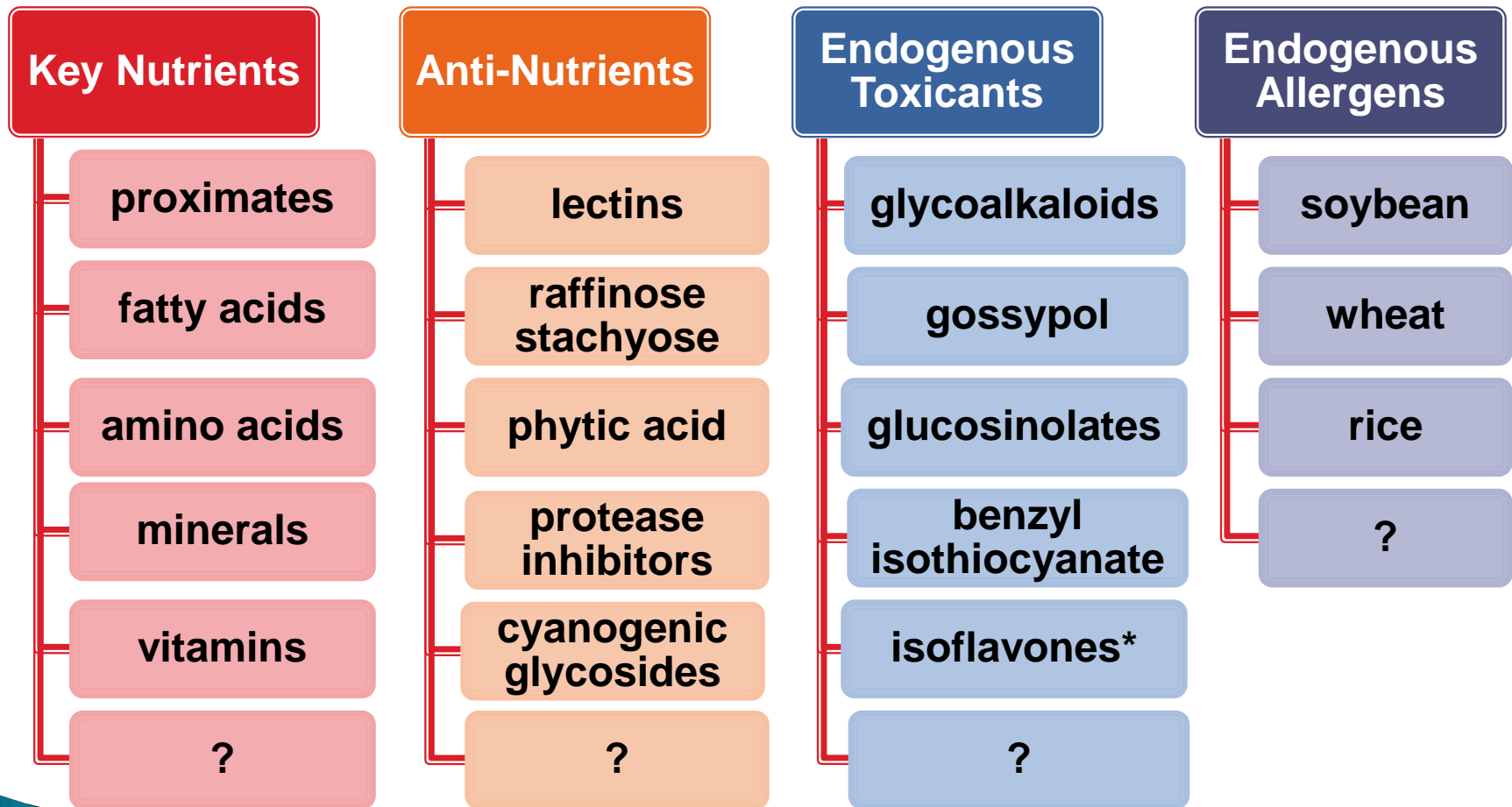
Endogenous Substances  
Must not contain  
substances at levels that  
are harmful

- Key components?
- Edible tissues? Raw or processed?
- Are there differences that raise safety questions?

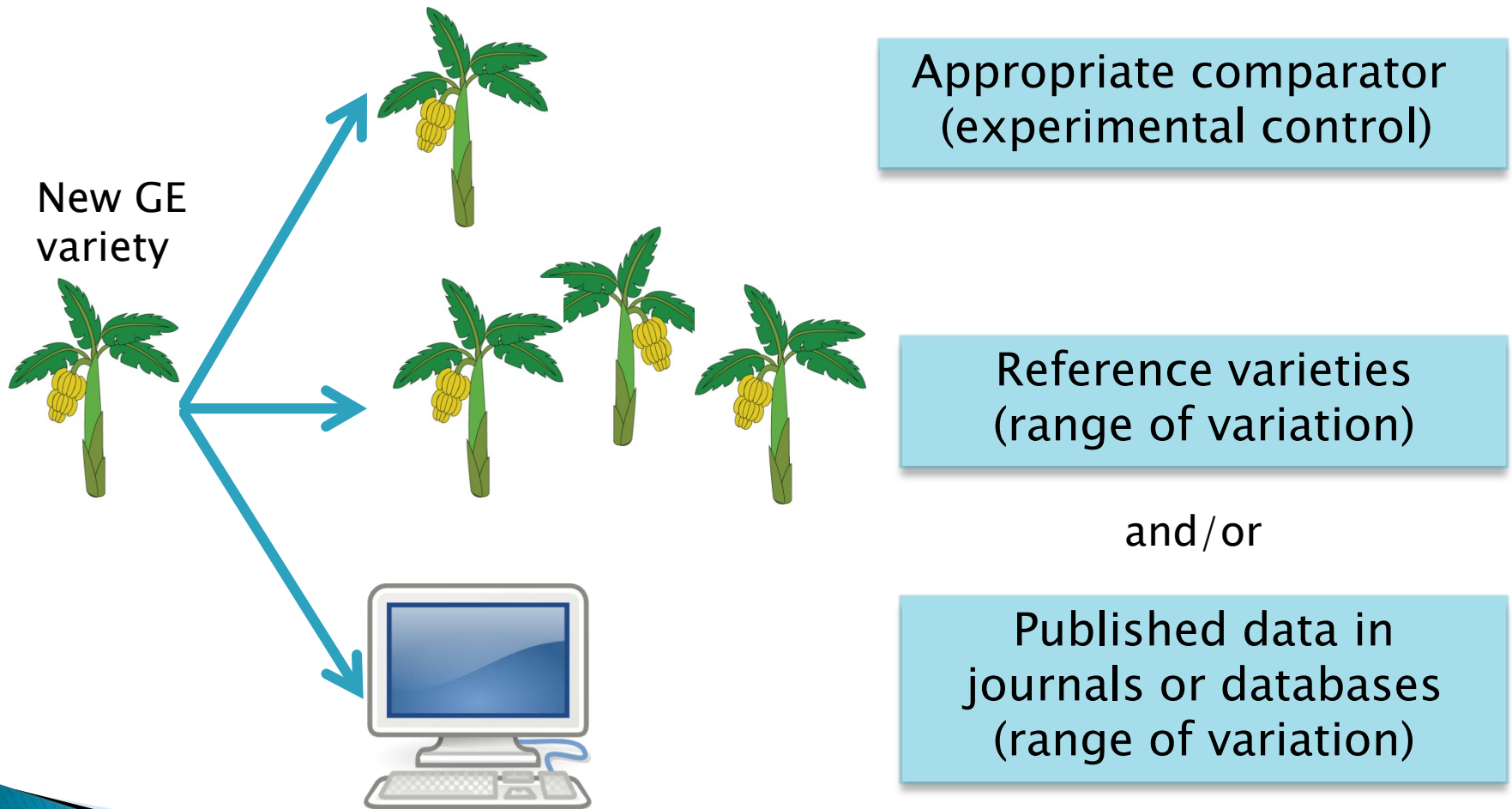


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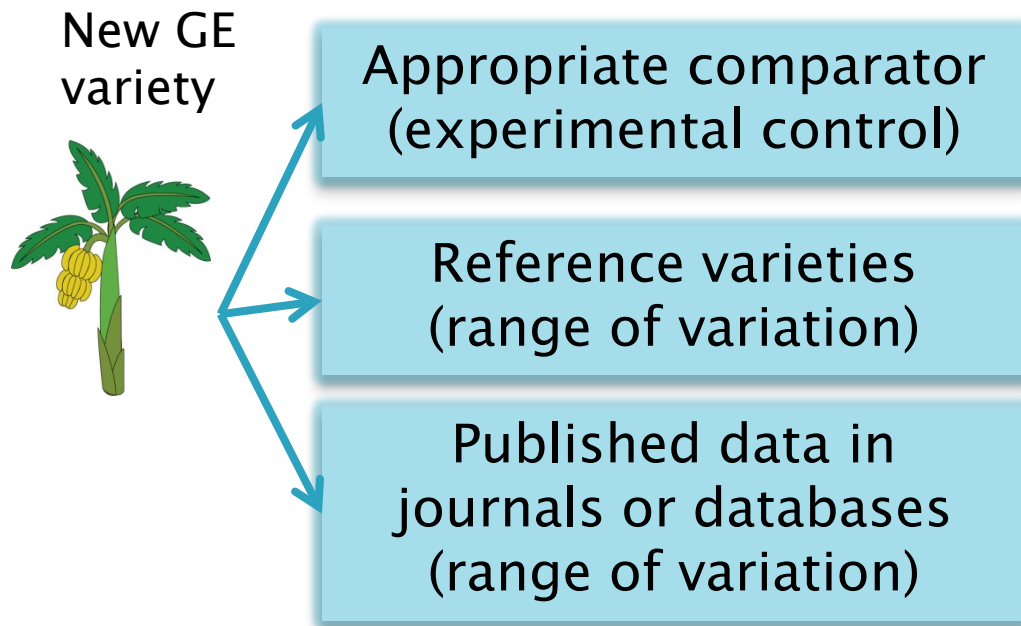
# Compositional assessment: key components



# Compositional Assessment: comparative approach



# Compositional Assessment: data evaluation



## Risk Assessment of Differences

- Are statistical differences biologically meaningful?
- Do any differences raise safety questions?
  - In the context of human or animal diets
  - Wholesomeness studies in livestock (if needed)



# Assessment of Added Substances

**Added Substances**  
Ingredients must meet safety criteria, may require FDA review and approval

- Toxicity
- Allergenicity
- New Metabolic Pathways



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# Safety assessment of added substances in GE crop

**Added Substances**  
Ingredients must meet safety criteria, may require FDA review and approval

## Potential for toxicity

- source of DNA
- bioinformatic comparison (proteins)
- function, digestibility, heat lability
- exposure
- oral toxicity studies (if needed)

## Potential for allergenicity

- source of DNA
- bioinformatic comparison
- digestibility and heat lability
- human serum testing (if needed)

## New Metabolic Pathway

- new/altered levels of substance(s) and information on ADME



# FDA's Approach to the Safety Assessment of Food from GE crops

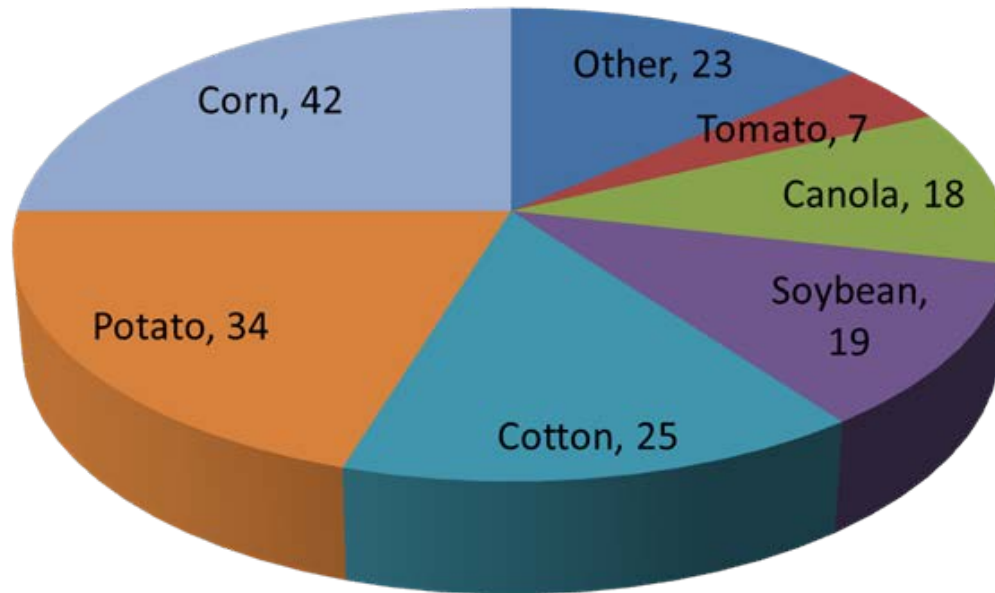
- ▶ **Case-by-case**
  - integrates history of safe use
- ▶ **Comparative approach**
  - evaluates biological relevance of statistical differences
- ▶ **Considers the safety of endogenous substances**
- ▶ **Considers the safety of added substances**
  - stepwise approach; weight of the evidence
- ▶ **Consistent with Codex Alimentarius**
  - *Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants*

# Biotechnology Consultations on Food from GE Plant Varieties

Biotechnology Consultations on Food from GE Plant Varieties				
<a href="#">FDA Home</a> <a href="#">Genetically Engineered Plants for Food &amp; Feed</a> <a href="#">Submissions on Bioengineered New Plant Varieties</a> <a href="#">Biotechnology Consultations on Food from GE Plant Varieties</a>				
<a href="#">Basic Search</a> <a href="#">Advanced Search</a>				
Search: <input type="text"/> <a href="#">Show Items</a> <a href="#">Clear</a>				
Records Found: 168 <a href="#">Show All</a> Page 1 of 4				
BNF No.	Traits	Food	Event Designation Unique Identifier	FDA Letter Date (sorted Z-A)
147	Altered Growth Properties	Corn	MON 87403 MON-87403-1	Jun 19, 2015
144	Insect Resistance	Soybean	MON 87751 MON-87751-7	May 27, 2015
132	Change in Composition (other)	Apple	GD743 OKA-NB001-8	Mar 20, 2015
132	Change in Composition (other)	Apple	GS784 OKA-NB002-9	Mar 20, 2015
141	Change in Composition (other)	Potato	F10 SPS-00F10-7	Mar 20, 2015

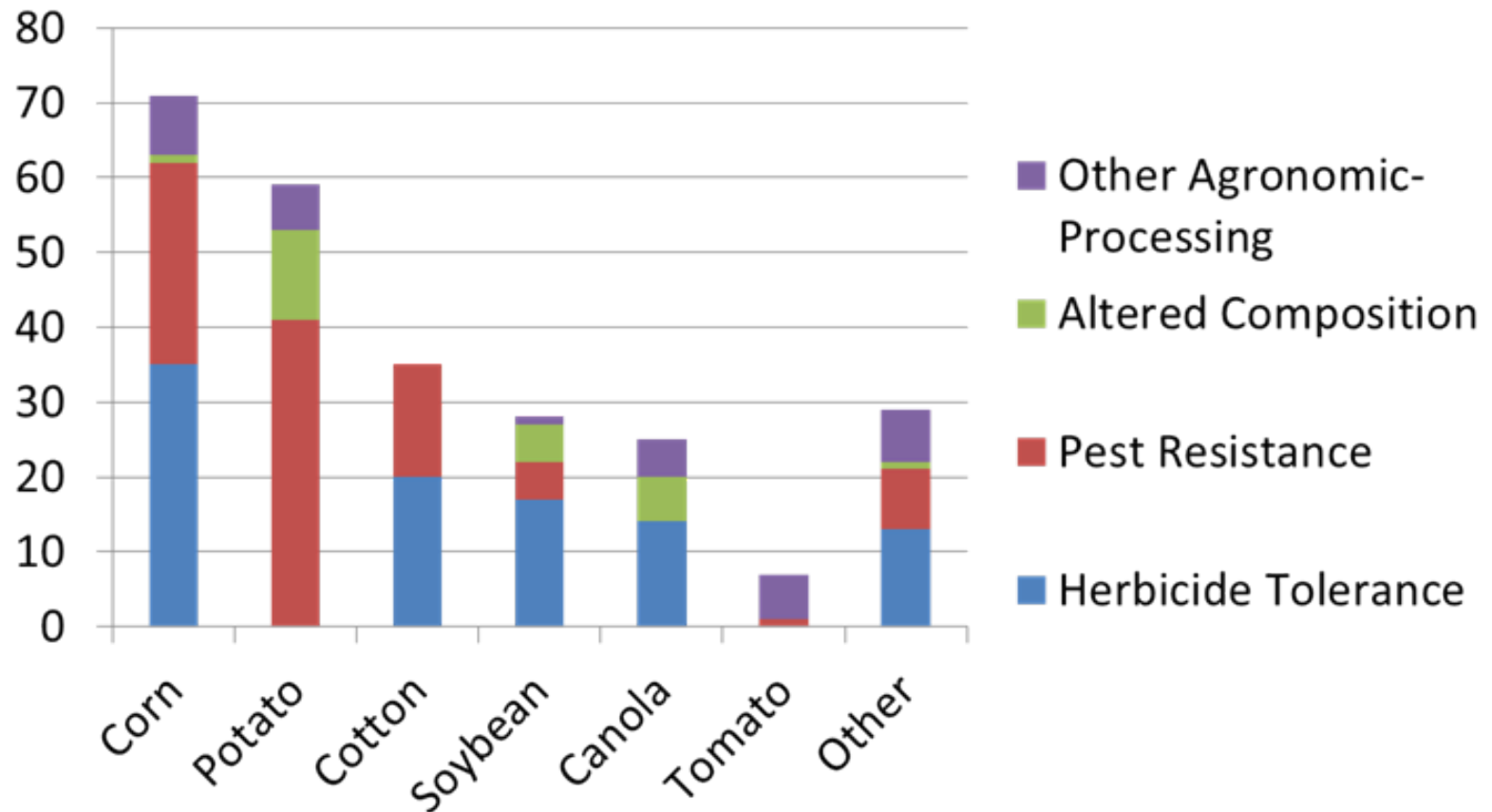
<http://www.fda.gov/bioconinventory>

# Evaluations to-date: number of events by crop



*\*Other ( $\leq 3$ ): alfalfa, radicchio, sugar beet, apple, cantaloupe, papaya, rice, squash, creeping bentgrass, flax, plum, wheat*

# Evaluations to-date: trait trends by crop



*\*Other: e.g., male sterility, female fertility, delayed ripening, delayed browning, reduced black spot, altered lignin profile*

# For More Information

## Internet:

FDA

<http://www.fda.gov/GEplantfoods>

## Email:

- FDA India Office..... [NDBoxFDAIndiaOffice@state.gov](mailto:NDBoxFDAIndiaOffice@state.gov)
- Biotech Program..... [Robert.Merker@fda.hhs.gov](mailto:Robert.Merker@fda.hhs.gov)
- NPC Program..... [Carrie.McMahon@fda.hhs.gov](mailto:Carrie.McMahon@fda.hhs.gov)