BACKGROUND INFORMATION

PART 1
New Variety Evaluation

A typical diet for most people includes a variety of foods. Some of those foods are eaten in their original form (such as a whole apple or a banana), while other foods (such as apple pie or banana muffins) are a combination of ingredients. Food ingredients include spices, sweeteners, preservatives, and other substances that affect food characteristics such as taste, texture, and nutritional content. The ingredients in processed foods are required to be on the labels.

All foods, whether a whole food or a food ingredient, have a certain chemical identity, i.e., a characterizing composition that may include one or more of the following: amino acids, fatty acids, carbohydrates, vitamins, and minerals (to name a few). Some whole foods and ingredients may also have components that function as anti-nutrients (compounds that interfere with nutrient absorption) or natural toxins. Some components may also elicit allergenic responses in susceptible people. The levels of these food components provide the food's specific identity, i.e., what makes a banana a banana or a salmon a salmon, and what distinguishes corn oil from olive oil.

When a **new plant variety** is developed through genetic engineering (GE plant, GE variety), its composition is typically analyzed and compared with parental and commercial varieties. The levels of key components (nutrients, anti-nutrients, and toxins) are compared to assess any significant changes in those components. The safety and effects of any new or added substances are also assessed. Depending on the nature of the new substance(s) and with its history in other foods, the types of safety data will vary. The results of this comparison support whether or not food from the new variety has essentially the same safety profile and nutrient content as food from traditionally bred plants.

Accurate labeling helps people know more about the nutritional profile and ingredients in the food they eat. Consumers can use this information to ensure that they get enough of the nutrients they need and understand how to limit nutrients they want to minimize. They also can use food labels to identify and avoid food allergens such as peanuts, milk, wheat, and other ingredients that can cause allergic reactions in some people. If a food or ingredient is from a GE plant, it's the plant that has been genetically engineered, and not the ingredient per se. Many ingredients to date (like starches, sugars, and oils) derived from GE plants do not contain recombinant DNA, RNA, or protein and are chemically and functionally identical to their non-GE-derived counterparts. New labeling for some foods containing ingredients made through genetic engineering (bioengineering) becomes effective in 2020 with compliance mandated by 2022.

What makes up a banana?

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).

Source: *Ingredients of an All-Natural Banana*, James Kennedy (VCE Chemistry teacher in Melbourne, Australia)

Safety Evaluation of Food from New Plant Varieties

The Federal Food, Drug, and Cosmetic Act requires that food from plants for humans and animals meet the same food safety requirements regardless of their origin, whether they are made from a plant variety that was created through crossbreeding, chemical or irradiation-induced mutagenesis, or genetic engineering. As new plant varieties were developed using GE tools over the past decades, FDA worked with the plant breeders to evaluate the safety of food from these GE varieties. This evaluation includes data analysis based on a comparison of food from the new GE plant variety to food from traditionally bred plant varieties with a history of safe use. Any differences identified during this comparison are then evaluated for safety.

BACKGROUND INFORMATION

Plant Biotechnology Consultation Program

FDA established a consultation process in the 1990s to work cooperatively with plant developers to help them ensure that foods made from new varieties, including those developed by genetic engineering, are safe and lawful. The consultation process allows a developer who intends to commercialize a new plant variety developed using modern genetic modification methods to meet with FDA to identify and discuss relevant safety, nutritional, or other regulatory issues about food for humans and animals made from the new variety. Plant breeders conduct tests and gather science-based evidence to verify that food from the new variety is as safe to eat as food from traditionally-bred varieties, and then submit the data and information to FDA for evaluation. FDA evaluates the submission and responds to the developer by letter. Since 1994, FDA has evaluated more than 180 new GE plant varieties through this program. For a list of completed consultations, see FDA's **Biotechnology Consultations database**.

Pre-market Consultation or Approval

Some food ingredients require FDA approval before marketing and some don't. A voluntary consultation process is one way for plant developers to check with FDA to see if food from the new plant variety contains a food additive that requires approval.

Safety Evaluation of GE Plants

Developers of GE plants gather information and conduct scientific studies to generate data, which they use to evaluate foods and ingredients from new varieties for safety and nutrition. Their review of food from the new varieties includes an examination of the following factors:

- **Identity**: Analyses to confirm the intended changes, including confirmation of the new or edited DNA, of new proteins produced from the DNA, and of other intended effects (traits).
- **Composition**: Whether key nutrients are within the expected ranges of values for the crop, whether endogenous (naturally occurring) toxins or antinutrients (compounds that interfere with the absorption of nutrients) are within acceptable levels
- **Safety and Regulatory Issues**: Potential for toxicity/allergenicity of new substances, and whether new substances require premarket review and approval by FDA by law. If the added substances are pesticides, they must be evaluated for food and environmental safety and authorized for use by the U.S. Environmental Protection Agency (EPA).

Identity

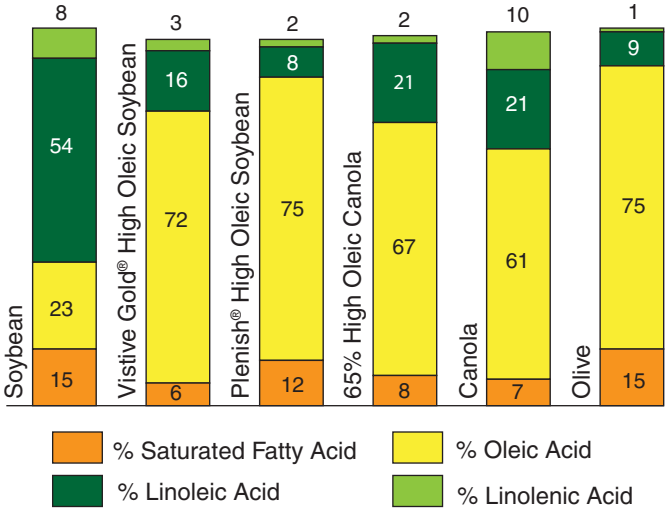
Developers of new plant varieties, including new GE varieties, collect data to identify distinguishing attributes of the new traits in the plant and assess whether any new proteins or components present in the new variety are safe for humans or animals to eat.

Developers of new GE varieties gather data to identify and assess attributes of food from the new variety. Their approach includes:

1. Recording detailed descriptions of the laboratory methods and results
2. Identifying the new, inserted, changed or edited DNA (this may include the use of DNA sequencing). This can include confirming that the intended genetic change occurred.
3. Identifying the new protein(s) created as a result of the genetic change (this may include the use of amino acid sequencing)
4. Measuring levels of new proteins or other substances produced in the plant and determining their levels in food (if present)

When a substance produced in a new GE plant variety is one that is already present at a comparable level in currently consumed foods, a safety question about the new substance is unlikely. For example, high oleic acid soybean oil has higher levels of oleic acid compared to typical soybean oils, but the higher levels are similar to other food oils, such as canola and olive oil.

Comparing Some Oils



Inform Magazine: High-oleic soybeans get the global green light, chart http://www.informmagazine-digital.org/informmagazine/april_2018/MobilePagedArticle.action?articleId=1367747#articleId1367747

When a substance produced in a new GE variety is one that is not present – or is present only at lower levels – in currently consumed foods, its safety in food must be evaluated.

BACKGROUND INFORMATION

Composition

Developers of new plant varieties, including new GE varieties, collect data on the composition of the new variety by conducting field trials. Field trials for new GE varieties frequently include the new GE variety (test), along with a genetically comparable plant variety as a control and possibly one or more commercial varieties as reference varieties. Samples from the edible parts of the test, control, and reference varieties are collected, and the levels of key nutrients, anti-nutrients, and toxins are measured.

The results of the compositional analysis for the new GE variety are then compared with the results for the control and reference varieties. They may also be compared with plant composition data in science journals and public databases.

Safety and Regulatory Issues

Health and Safety

New substances present in food from the new plant varieties, such as those introduced by genetic engineering, are studied to determine whether they could be toxic or allergenic. One way to determine if a new protein from the GE plant has the potential to be toxic or allergenic is to compare its amino acid sequence for similarity to those of known toxins and allergens. Another way is to consider whether the source of the DNA encoding the new protein is toxigenic or allergenic. The safety of substances that are not proteins can be evaluated, for example, through:

- scientific principles, such as whether the substance has historically been safely consumed in the diet and the similarity of the substance to other substances safely consumed in the diet
- dietary exposure estimate
- knowledge of their digestive fate once consumed
- data from toxicity studies of the substance

The composition of food from new plant varieties is also evaluated for meaningful changes in their nutritional values or increased levels of endogenous anti-nutrients or toxins. Plants are an important source of nutrients in the diet, so changes in their composition have the potential to impact the health of humans and animals. Some plants that we eat also produce natural toxins that are usually defense molecules against environmental threats such as bacteria, fungi, insects, or predators. Two examples of natural toxins are glycoalkaloids in potatoes and psoralens in celery. These natural toxins are generally not present in domesticated food crops at levels high enough to affect human or animal health, but breeding may lead to changes in the levels of these substances.

Compositional changes are evaluated by dietary experts for their potential to impact the health of humans or animals. In some cases, the compositional change is specifically made to improve dietary intake status. For example, Golden Rice was developed to address vitamin A deficiency in south and southeast Asian countries where people typically consume a rice-based diet. However, if the level of a nutrient in the new plant variety is found to be too low or too high, this could lead to dietary deficiency or excess, respectively. Likewise, if the level of an anti-nutrient or toxin is found to be too high, this could cause harm. Either way, it is important to conduct the analysis in the context of the total diet. Scientists consider the role of food from the plant in the diet of humans and animals when performing this analysis. For example, they consider whether the food is an important source of particular vitamins and minerals in the context of the total diet.

Long-Term Safety

Scientists with expertise assessing the long-term safety of food and food ingredients for humans and animals consider several factors when they evaluate food from new plant varieties, including new GE varieties. This includes information about the long-term safety of the food from traditionally bred crops and information about the food safety of the newly introduced traits. The plant's components (fiber, protein, fat, DNA, anti-nutrients, etc.) have typically been part of the human diet for thousands of years. Just like the plant's endogenous nucleic acids and proteins, the recombinant nucleic acids and proteins are degraded during digestion in the human or animal gastrointestinal tract into their building blocks. For all GE plant varieties evaluated to date through FDA's Plant Biotechnology Consultation Program, the long-term safety of food from the new GE variety is expected to be the same as that of food from comparable traditionally-bred and safely-consumed plant varieties.

Note: When FDA considers the safety of foods from a new plant variety, it considers uses of the plant in food for both humans and animals.

BACKGROUND INFORMATION

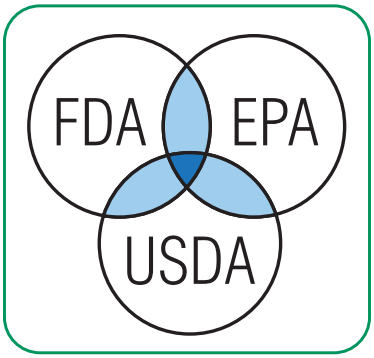
Developer's Assessment

Developers of new plant varieties evaluate safety, nutritional, and other regulatory issues. The developers may choose to submit a summary to FDA describing their approach. For new GE varieties, the summary usually includes:

1. The name of the food and the crop from which it is derived
2. A description of how the food will be used, including animal food uses
3. The sources, identities, and functions of introduced genetic material
4. The purpose or intended technical effect of the modification, and its expected effect (if any) on the composition or characteristic properties of the human or animal food
5. The identity and function of expression products (new proteins or RNA) encoded by the introduced genetic material, including an estimate of the concentration of any expression product in the new GE variety or derived food
6. The basis for concluding that foods containing the expression products can be safely consumed, including information showing the expression products are not toxins or allergens
7. A comparison of the composition of food from the new variety with that of food from the original parental variety or other commonly consumed varieties, particularly nutrients and toxins that occur naturally in the food
8. A discussion of available information addressing whether the potential for food from the new variety to induce an allergic response has been altered by the genetic modification
9. Any other information relevant to the safety and nutritional assessment of the food from the new GE variety.

A team of FDA scientists with expertise in food safety and nutrition for humans and animals reviews the developer's data, and asks the developer to clarify or answer questions about their data. FDA reviews the developer's responses and continues asking questions until no further questions remain. FDA prepares an evaluation summary and sends the developer a letter stating the agency did not identify any safety or regulatory issues requiring further evaluation and reminding them that they remain legally obligated to ensure the safety of the final products they bring to market. For more Information, see FDA's Fact Sheet:
New Plant Variety Regulatory Information
https://www.fda.gov/food/food-new-plant-varieties/new-plant-variety-regulatory-information

Coordinated Biotechnology Regulation



Three federal agencies (FDA, USDA, and EPA) act under a coordinated regulatory framework to ensure the overall safety of GE new plant varieties:

- FDA regulates the safety of all food products for humans and animals in the United States other than meat, poultry, catfish and certain egg products, which are regulated by USDA.
- USDA, specifically the Animal and Plant Health Inspection Service (APHIS), is responsible for protecting agriculture from pests and diseases. They supervise field testing and monitor GE seed distribution until the GE plant variety is shown not to be harmful to agriculture and the environment.
- EPA regulates pesticides, including those that are produced in plants as a result of genetic engineering. To protect human and animal health, EPA assures that pesticidal substances expressed in GE plants are safe for consumption. EPA also regulates the environmental safety of the pesticidal substances.

To learn more about each agency's role, explore the resources below.

- Coordinated Framework: **https://usbiotechnologyregulation.mrp.usda.gov/biotechnologygov/home**
- FDA: *Food from New Plant Varieties* **www.fda.gov/Geplantfoods**
- USDA: *Regulation of Biotechnology* **https://www.aphis.usda.gov/aphis/ourfocus/biotechnology**
- EPA: *EPA's Regulation of Biotechnology for Use in Pest Management* **https://www.epa.gov/regulation-biotechnology-under-tsca-and-fifra/epas-regulation-biotechnology-use-pest-management**

GE Animals

GE animals can be developed for a variety of purposes including disease-resistance, improved nutritional composition (e.g. healthier fat or lower allergenicity), and greater productivity (faster growth with less feed). For example, AquAdvantage Salmon was genetically altered to grow more quickly, using a gene commonly found in another type of fish. This salmon is the first GE animal to be approved for human consumption.

BACKGROUND INFORMATION

Scientific Perspectives

The scientific consensus is that food from GE plant varieties available for consumers are safe, i.e., pose no greater health risks or environmental concerns than their non-GE counterparts.

Some of the scientific organizations that support this position are:

- FDA, USDA, and EPA
- National Research Council
- American Association for the Advancement of Science
- Council on Science and Public Health
- World Health Organization
- European Food Safety Authority

Evolving Science

More technologies emerge as farmers and scientists address changing needs in food agriculture. One approach, genome editing, describes a relatively new set of techniques to make changes at specific locations in the DNA of a plant, animal, or other living organism. (See Module 2.) These technologies can be used to introduce, remove, or substitute one or more specific nucleotides at a specific site in the organism's genome. Examples of different genome editing techniques include clustered regularly interspaced short palindromic repeat associated nucleases (CRISPR), zinc-finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and oligonucleotide-directed mutagenesis (ODM). FDA completed its first voluntary food safety consultation on food derived from a plant produced using genome editing in February 2019. Regardless of how a plant is produced, food from the plant must be safe.

Examples of Foods Made with GE Techniques

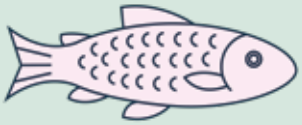
Plant

- USDA Approves Genetically Modified Non-Browning Apple (Arctic® Apples) **www.youtube.com/watch?v=3LFmWhJu6Pw**

AquAdvantage Salmon

- AquAdvantage Salmon is the first GE animal for consumption with an FDA-approved application. The company collected data for over 10 generations of the animal.

Read the FDA AquAdvantage Salmon Fact Sheet: **https://www.fda.gov/animal-veterinary/animals-intentional-genomic-alterations/aquadvantage-salmon-fact-sheet**



Federal agency inventories of safety evaluations

(search by product, e.g., apple):

- FDA: **https://www.fda.gov/food/consultation-programs-food-new-plant-varieties/final-biotechnology-consultations**
- USDA: **https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions/petitions/petition-status**
- EPA: **https://www.epa.gov/ingredients-used-pesticide-products/current-and-previously-registered-section-3-plant-incorporated**

DID YOU KNOW?

FDA and USDA use different words to characterize the regulatory processes by which a GE plant is evaluated and designated as safe. FDA uses a consultation process to evaluate whether food from a GE plant requires FDA's premarket approval for safe use. USDA uses a petition process to deregulate (remove from USDA's regulatory oversight) GE plants once it is determined they do not pose a plant pest risk.

Three-Part, Science-Based Approach to Safety Evaluation of New Plant Varieties

Case-by-case approach	Comparative approach	Focus on new substances
Does the plant have a history of safe use? Is it typically used in human food? In animal food? What parts of the plant are eaten? Is it eaten fresh or is it processed?	Are the levels of important nutrients in food from the plant similar to the levels in food from varieties of the plant with a history of safe use? Are the levels of toxins and anti-nutrients the same or lower? If the levels are different, do the differences affect safety or nutrition?	Are there new substances in the plant? Will the new substances be present in food made from the new plant? If so, are the new substances toxins, antinutrients, or allergens?

SAFETY EVALUATION PROCESS FOR NEW PLANT VARIETIES