FOODS : PAST, PRESENT AND FUTURE

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Our Foods Always Looked Like They Do Today, Right?

No. Why?

Carrot

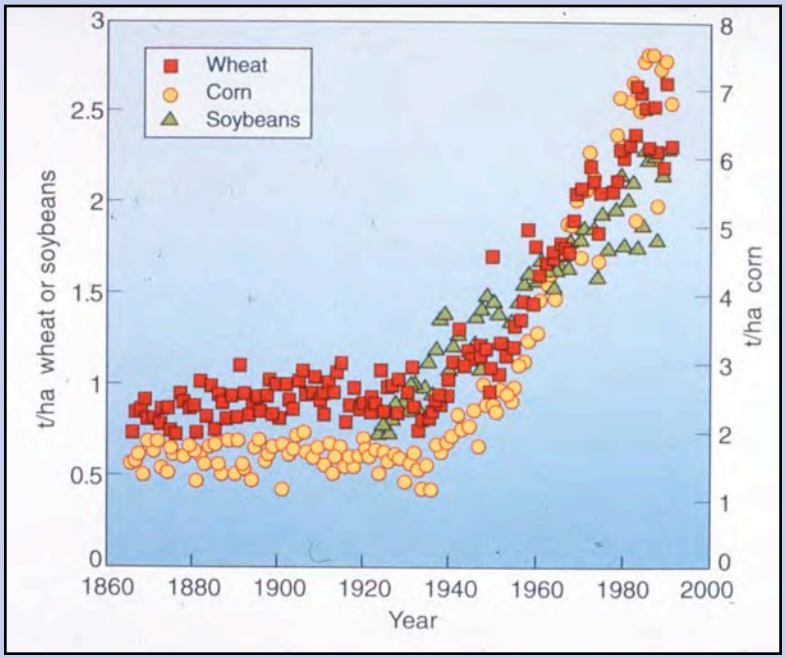
Eggplant

Banana

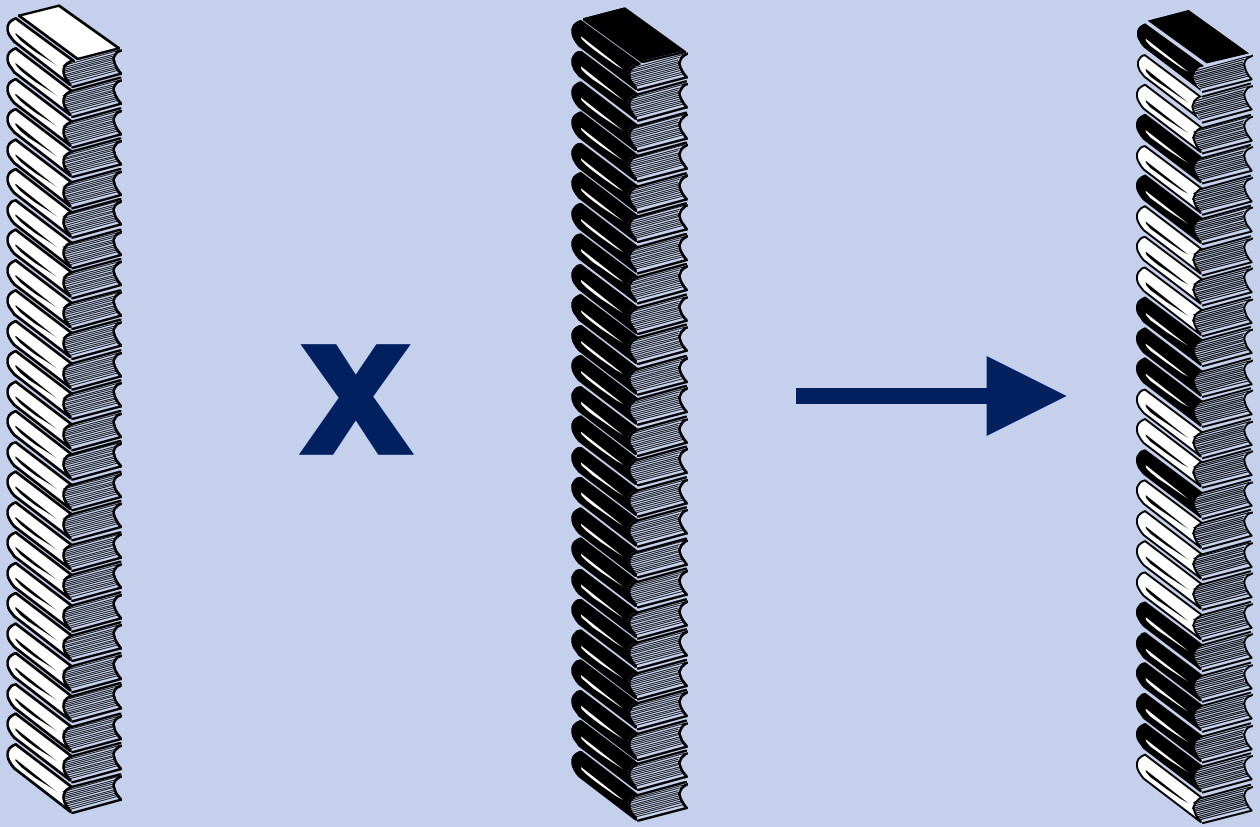
Broccoli,
Kale,
Cabbage

One reason: intentional mutation breeding used since 1950s leading to >3200 officially released crops, e.g., 600 maize, rice, wheat varieties. Although modified genetically, they are not regulated like genetically engineered (GE, GMO) varieties.

Another reason: hybridization or cross breeding. This can be unintentional via wind or bees or intentional via human intervention.



What happens in that process? - example wheat



1700 books
(or 1.7 million pages)

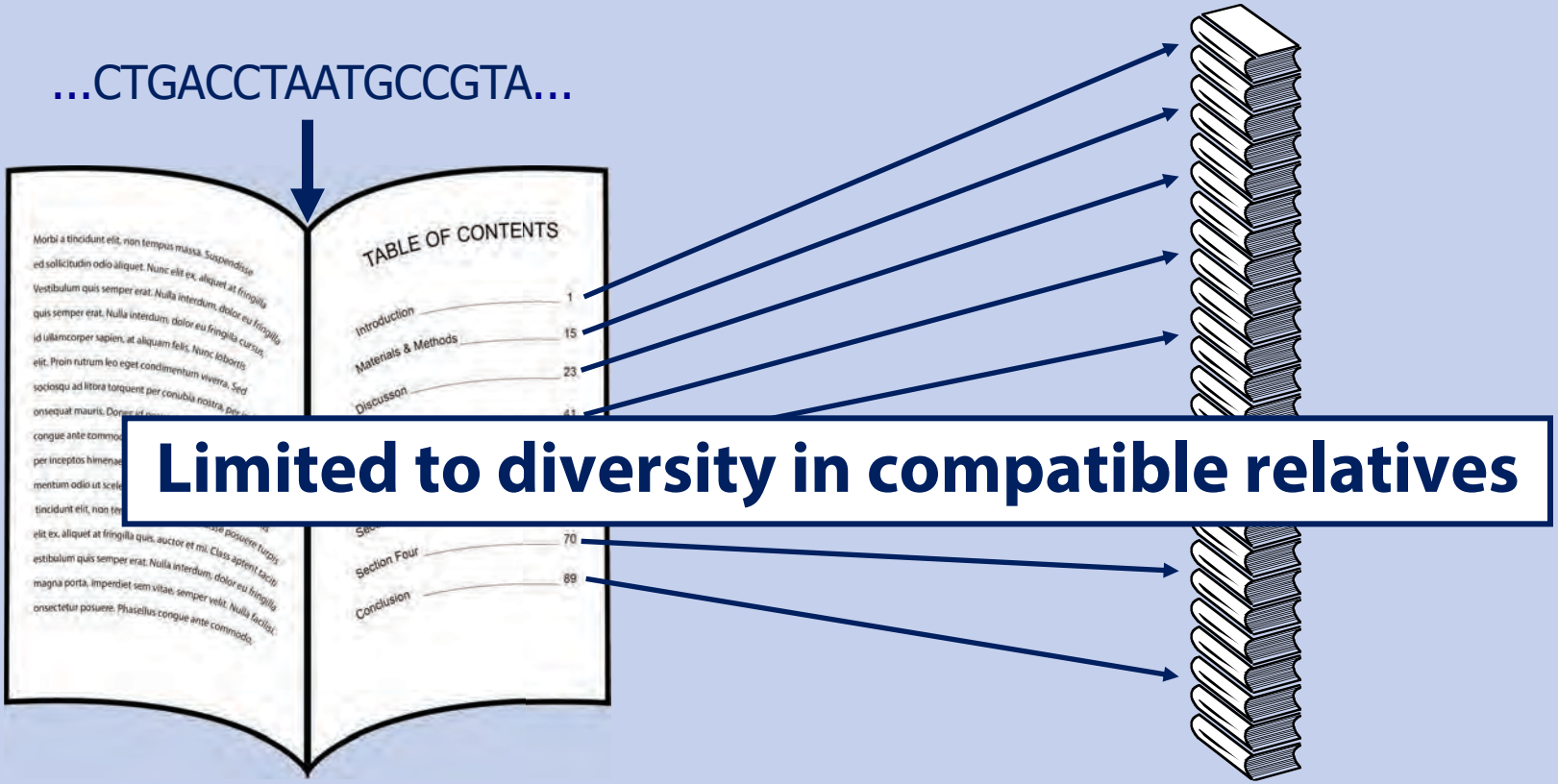
1700 books
(or 1.7 million pages)

1700 books
(or 1.7 million pages)

Random retention of information from each parent

Genetic modification by hybridization is not GE or GMO

Another way to modify genomes: breeders use a table of contents for genes

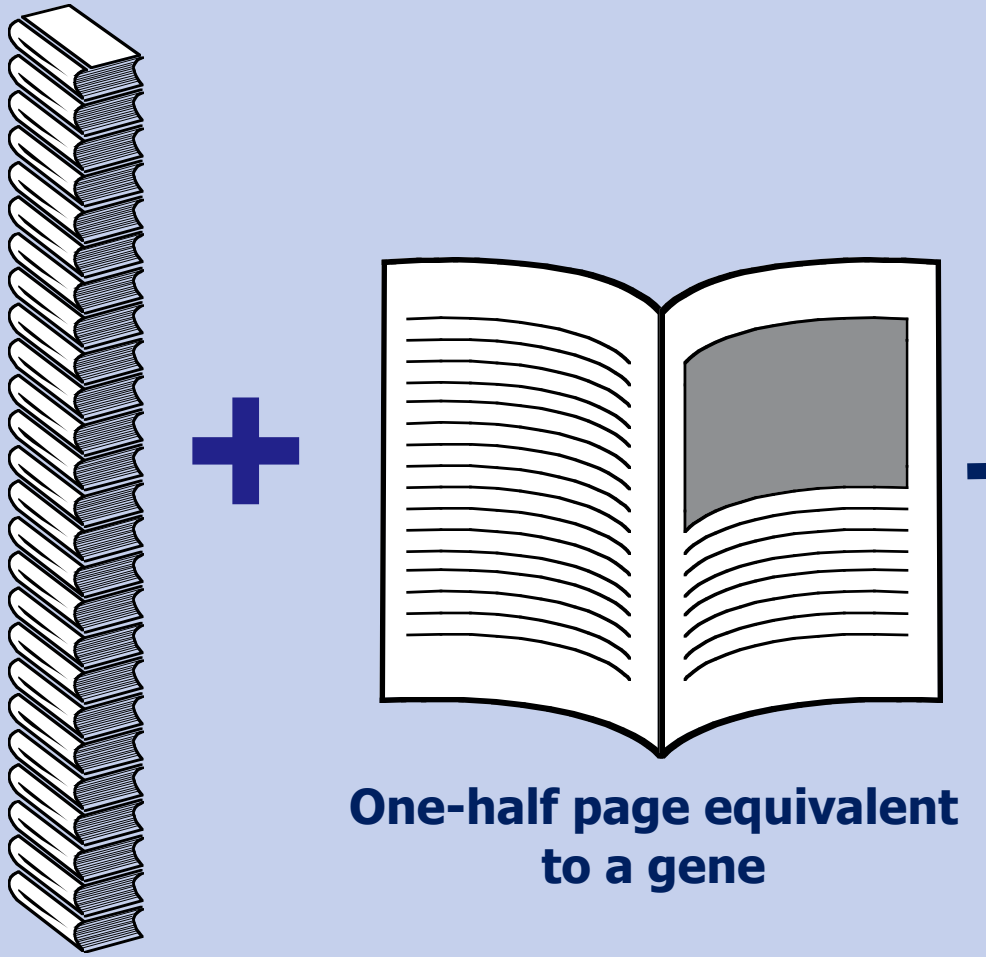


Limited to diversity in compatible relatives

1700 books
(or 1.7 million pages)

Genetic modification that <u>is not</u> GE or GMO

Another way to modify: Genetic Engineering



1700 books
(or 1.7 million pages)

One-half page equivalent
to a gene

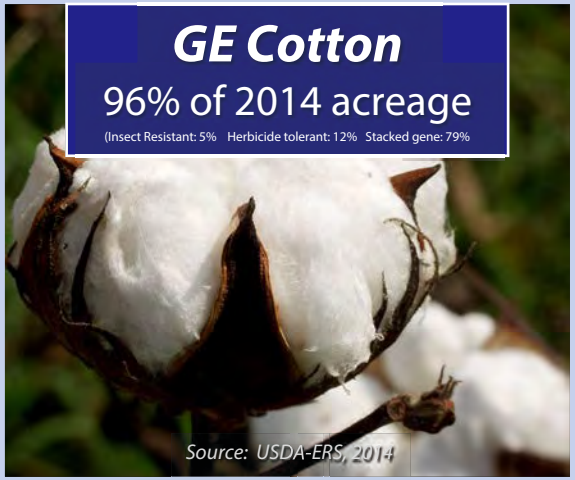
Inserts
randomly in
genome

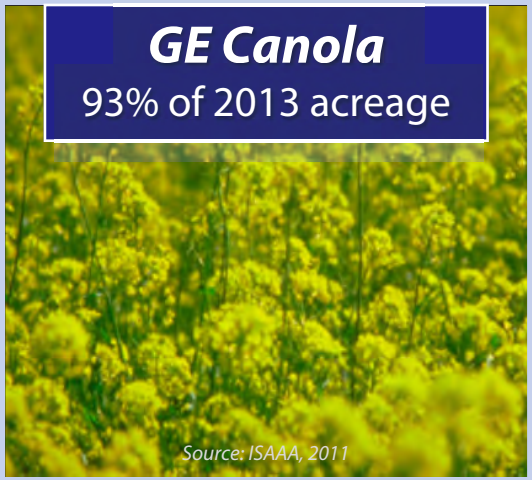
Inserted
gene(s)

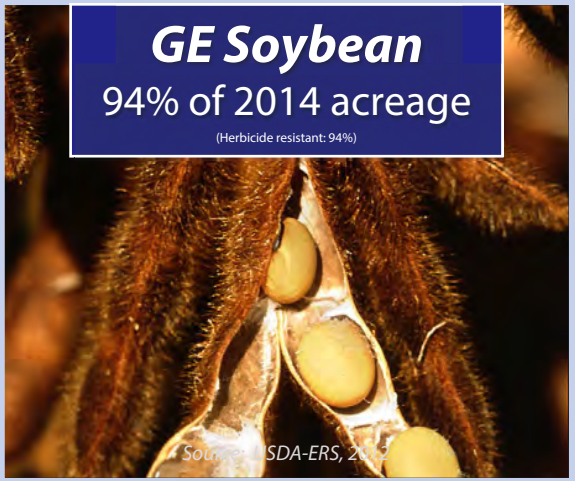
1700 books
(or 1.7 million pages)

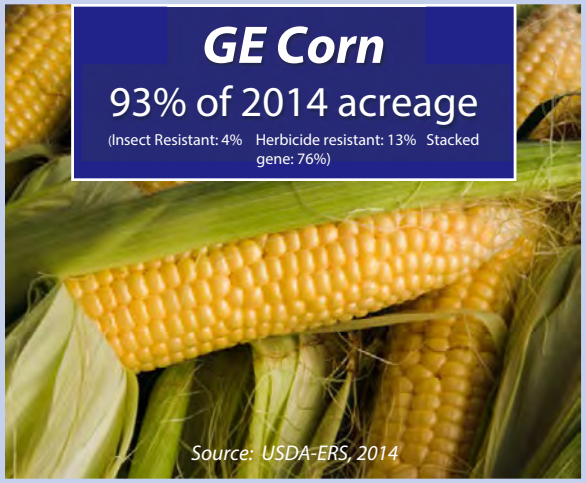
Genetic modification by genetic engineering <u>is</u> GE or GMO

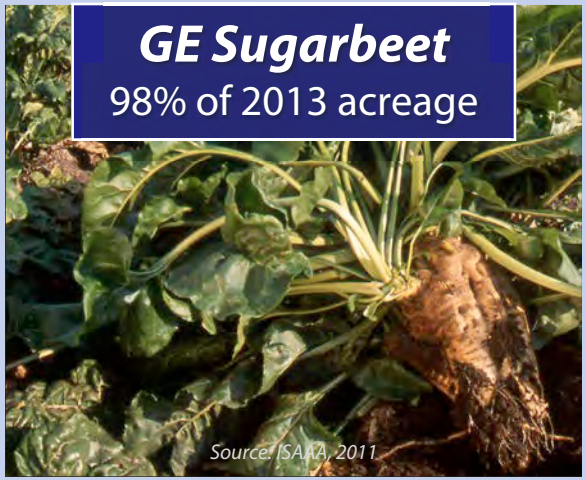
Number of different commercially available, large acreage GE (GMO) crops is limited

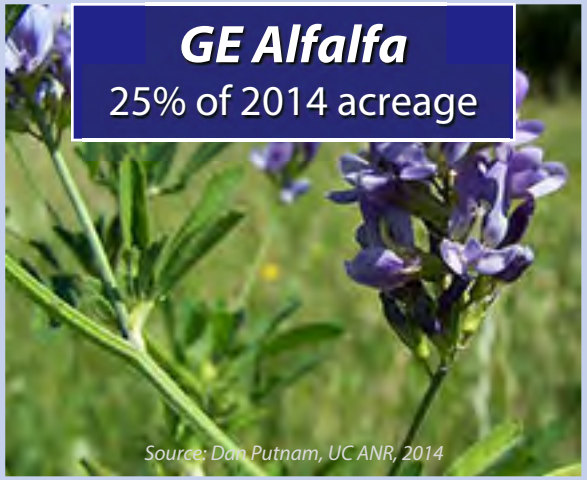










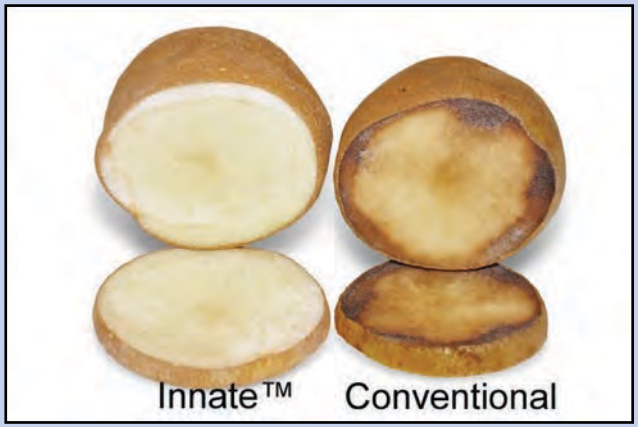


Only a few whole, GE (GMO) foods are in the commercial U.S market

Two more have been approved

Arctic Apple™

Introduced in 400 Midwest stores in Oct. 2017



Innate™ Potato

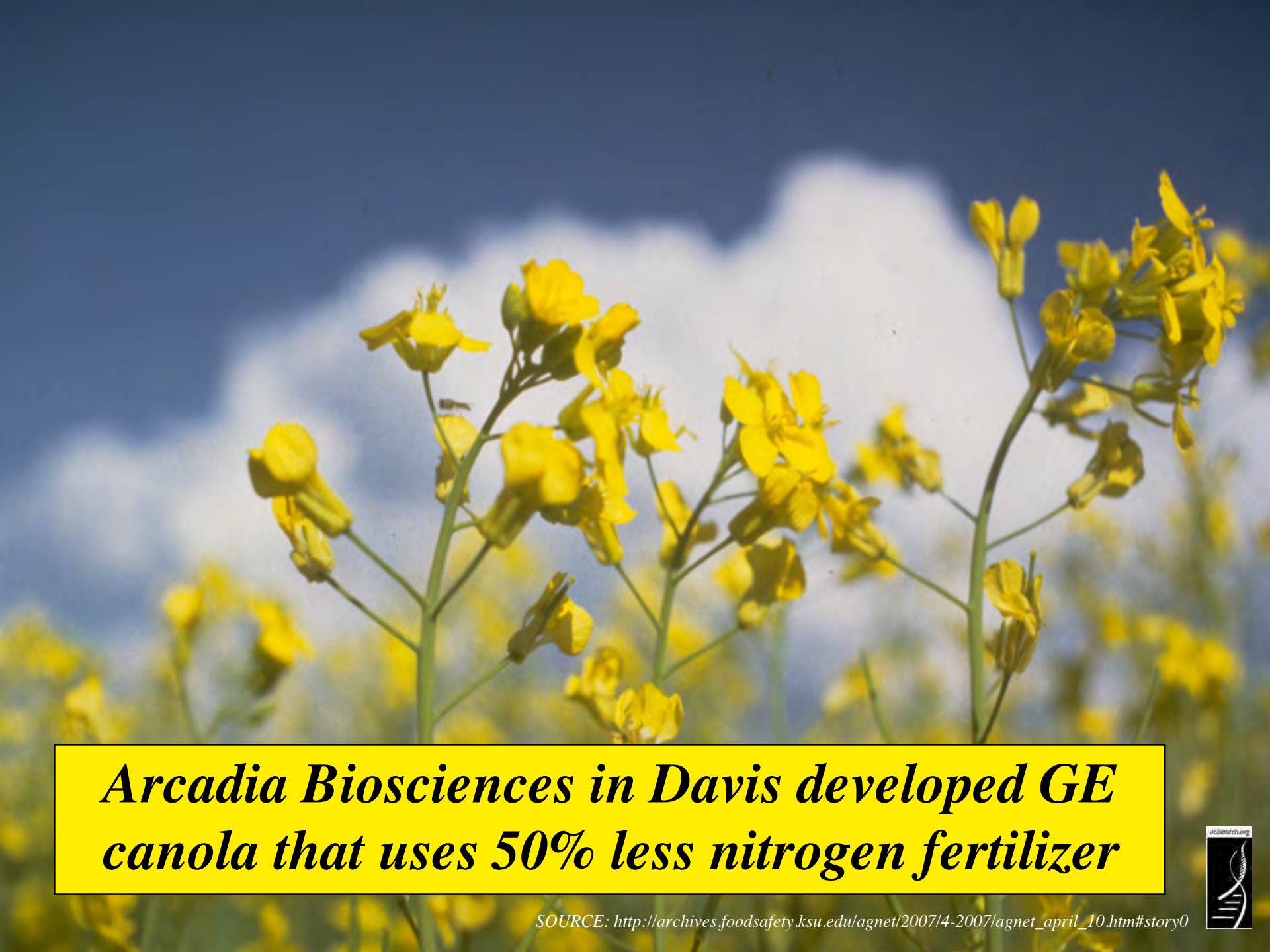
Number of different traits available in large acreage, GE (GMO) crops also limited

Bt Crops - engineered for insect resistance

Herbicide-tolerant (HT) - engineered to tolerate herbicide application

There are also stacked Bt plus HT varieties

Many more engineered crops in the pipeline



Arcadia Biosciences in Davis developed GE canola that uses 50% less nitrogen fertilizer

SOURCE: http://archives.foodsafety.ksu.edu/agnet/2007/4-2007/agnet_april_10.htm#story0

Late blight tolerant GE potato field study in Ireland: engineered with gene from wild potato variety

amiga
Assessing and Monitoring the Impacts of Genetically modified plants on Agro-ecosystems

teagasc
Agriculture and Food Development Authority

WAGENINGEN UR
For quality of life

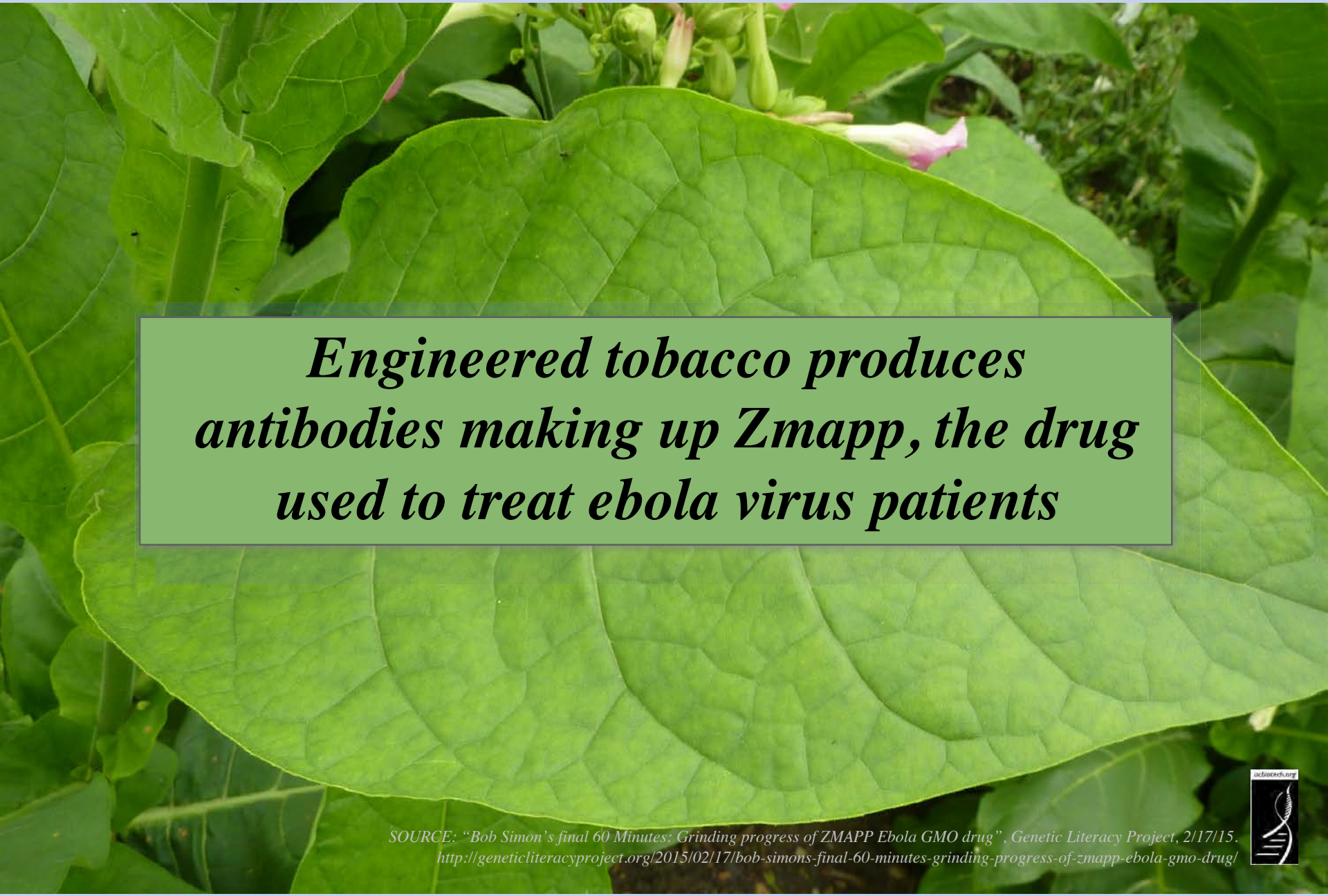
ucbiotech.org

American chestnuts engineered with a wheat gene to prevent cankers; replanted by community with $104K raised through crowd funding campaign

http://www.newscientist.com/article/dn25644-american-chestnut

High anthocyanin purple GE tomatoes. Diets with 10% purple tomatoes increased lifespan of cancer-prone mice

Butelli et al. 2008. https://www.jic.ac.uk/staff/cathie-martin/purple-tomatoes.html



Engineered tobacco produces antibodies making up Zmapp, the drug used to treat ebola virus patients

SOURCE: "Bob Simon's final 60 Minutes: Grinding progress of ZMAPP Ebola GMO drug", Genetic Literacy Project, 2/17/15.
http://geneticliteracyproject.org/2015/02/17/bob-simons-final-60-minutes-grinding-progress-of-zmapp-ebola-gmo-drug/

What is regulatory structure for GE/GMO crops and foods?

U.S. Agencies Regulating GE Crops/Foods

USDA

- Field testing
  - -Permits
  - -Notifications
- Determination of non-regulated status

Plant pest?

FDA

- Food safety
- Feed safety

Danger to people?

EPA

- Pesticidal plants
  - -tolerance exemption
  - -registrations
- Herbicide registration

Risk to environment?

USDA variety release requirements for conventional varieties require data on:

- **agronomic performance**
- **proximate analysis**
- **antinutritive factors**

Paperwork required for registration of conventional flax variety

A. McHughen,
UC Riverside

USDA variety release requirements for engineered varieties require that data plus…

Paperwork required for registration of GE flax variety

A. McHughen
UC Riverside

- Molecular characterization of inserted DNA,
- Southern and restriction analyses
- PCR for several fragments,
- Various enzyme assays (ALS, NOS, NPT-II)
- Copy number of inserts
- Size of each fragment,
- Source of each fragment
- Utility of each fragment
- How fragments were recombined
- How construct was delivered into flax
- Biological activity of inserted DNA (genes)
- Quantitative analyses of novel proteins (western analyses)
- Temporal activity of inserted genes
- Spatial activity of inserted genes
- Complete amino acid analysis
- Detailed amino acid analysis for valine, leucine and isoleucine
- Toxicity
- Allergenicity
- Biological analysis:
- Pathogenicity to other organisms
- Dormancy,
- Outcrossing
- Potential for horizontal gene transfer
- Seed production
- Flowering time,
- Flower morphology
- Analysis of relatives
- Stability of inserted genes over seed generations
- Survivability in natural environment
- Survivability in agricultural environment in presence of herbicide
- Survivability in agricultural environment in absence of herbicide
- Interaction with other organisms- alterations to traditional relationships
- Interactions with other organisms- novel species
- Changes to persistence or invasiveness
- Any selective advantage to the GMO
- Any selective advantage to sexually compatible species
- Plan for containment and eradication in the event of escape

Not cheap. Industry estimates costs are $10-$20M for each event! Beyond resources of academics and small companies

Regulatory system same since 1986, minor revisions in 1992, resulting in:

- **New products emerging with no rules to govern them;**
- **No clear commercialization path for older products;**
- **New products made to avoid regulation, by not using plant pest parts.**

USDA APHIS created new regulations for GE wheat after finding GE varieties in Oregon and Montana - where they shouldn't have been

Must be field tested **under permit process rather than notification process, requiring, e.g., more monitoring and reporting**.

1. **Plants and plant parts must be contained or devitalized**.
2. **Regulated article must not persist in environment**.
3. **Upon termination of field test, no viable material shall remain.**

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MIT Technology Review

Chinese Researchers Stop Wheat Disease with Gene Editing

Researchers have created wheat that is resistant to a common disease, using advanced gene editing methods.

By David Talbot on July 21, 2014

Advanced genome-editing techniques have been used to create a strain of wheat resistant to a destructive fungal pathogen – called powdery mildew – that is a major bane to the world's top food source, according to scientists at one of China's leading centers for agricultural research.

And then there is editing… and how are these crops regulated?

Advanced genome-editing techniques used to create wheat resistant to powdery mildew by deleting genes that repress defenses against mildew

SOURCE: "Chinese Researchers Stop Wheat Disease with Gene Editing", MIT Technology Review, July 21, 2014
http://www.technologyreview.com/news/529181/chinese-researchers-stop-wheat-disease-with-gene-editing/

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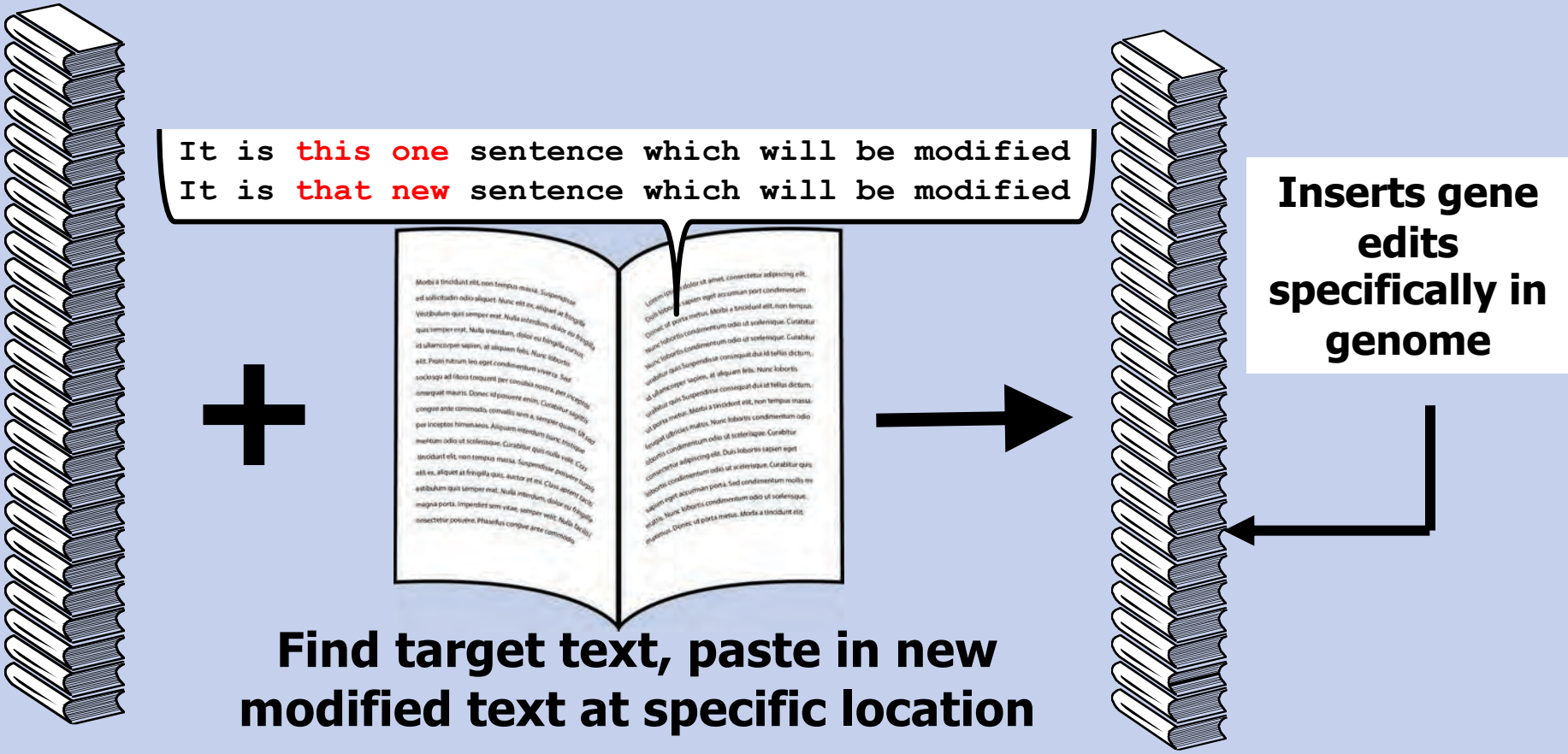
New Genetic Method: Genome Editing-1



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This type of genome editing *is not* GE or GMO under current USDA regulation, if deletions or small base changes; FDA & EPA unknown

EXAMPLES of such edited products:

nature

NATURE | NEWS

Gene-edited CRISPR mushroom escapes US regulation

Jose A. Bernat Bacete/Getty Images

University

Dupont Develops Corn Using New CRISPR Technology

By KRISTOFOR HUSTED • APR 27, 2016

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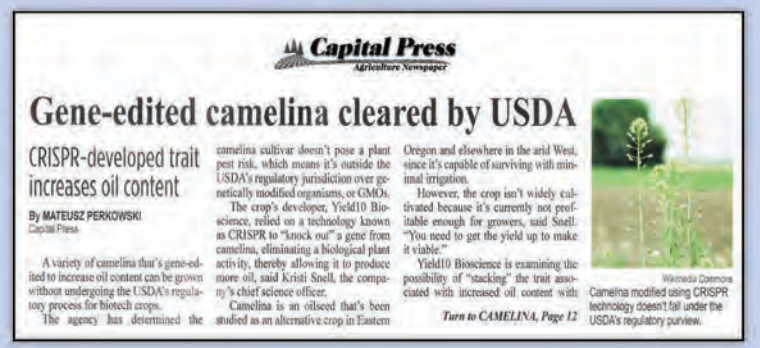
LIZ WEST, FLICKR CREATIVE COMMONS

A new genetically engineered corn variety developed by one of the world's largest seed companies won't undergo the same review by regulators as other GMO crops.

Company



Capital Press

Agriculture Newspaper

Gene-edited camelina cleared by USDA

CRISPR-developed trait increases oil content

By MATEUSZ PERKOWSKI

Capital Press

A variety of camelina that's gene-edited to increase oil content can be grown without undergoing the USDA's regulatory process for biotech crops.

The agency has determined the camelina cultivar doesn't pose a plant pest risk, which means it's outside the USDA's regulatory jurisdiction over genetically modified organisms, or GMOs.

The crop's developer, Yield10 Bioscience, relied on a technology known as CRISPR to "knock out" a gene from camelina, eliminating a biological plant activity, thereby allowing it to produce more oil, said Kristi Snell, the company's chief science officer.

Camelina is an oilseed that's been studied as an alternative crop in Eastern Oregon and elsewhere in the arid West, since it's capable of surviving with minimal irrigation.

However, the crop isn't widely cultivated because it's currently not profitable enough for growers, said Snell. "You need to get the yield up to make it viable."

Yield10 Bioscience is examining the possibility of "stacking" the trait associated with increased oil content with

Turn to CAMELINA, Page 12

Wikimedia Commons

Camelina modified using CRISPR technology doesn't fall under the USDA's regulatory purview.

Company

Capital Press

USDA won't regulate biotech wheat variety

Cultivar modified to 'knock out' mildew-susceptible gene

By MATEUSZ PERKOWSKI

Capital Press

A wheat variety rendered mildew-resistant through the targeted "knockout" of a gene can be commercialized without clearing USDA regulatory hurdles for biotech crops.

The agency's Animal and Plant Health Inspection Service has found that the cultivar doesn't fall under its jurisdiction for regulating genetically engineered crops, which is limited to possible plant pests and pathogens.

While the wheat was developed with genetic elements from gene-editing bacteria, they aren't contained in the crop and thus it's not subject to USDA's deregulatory process, which includes environmental analysis and public comment, according to APHIS.

Capital Press file photo. The Animal and Plant Health Inspection Service has found that a new mildew resistant wheat cultivar doesn't fall under its jurisdiction for regulating genetically engineered crops.

Most biotech crops commonly grown in the U.S. have undergone deregulation, and in some cases, lawsuits over the adequacy of this process have delayed their commercialization.

Calyxt, a subsidiary of the biopharmaceutical company Cellectis, developed "MLO_KO" wheat with genetic sequences from bacteria and corn that remove a gene that suppresses the plant's defenses against powdery mildew.

The wheat's DNA is repaired during natural cellular processes and no foreign genetic material remains.

"It does not change the wheat's basic biology or produce a plant that would directly feed on, infect, parasitize, or contaminate plants, or adversely affect other organisms that are beneficial to plants," Calyxt said in a letter to APHIS.

The gene eliminated by Calyxt is involved in the plant's biological processes but the mildew fungus also relies on it to "trick" and penetrate the wheat cell, said Luc Mathis, the company's CEO.

Even without the gene, the wheat's biology remains unaffected due to other genes that perform duplicative roles, he said. "When you remove this function, the plant behaves normally."

Though the USDA has decided the wheat cultivar can be commercialized, Mathis said he doesn't expect the crop to be sold to farmers until 2022.

Calyxt must first conduct trials to ensure the trait is reliable in the field while simultaneously incorporating the mildew resistance into geographically suitable wheat varieties, he said.

Turn to WHEAT, Page 12

Company

In 2016/2017, USDA APHIS: can't regulate corn, mushroom, wheat, camelina made with genome editing because no DNA from plant pest, pathogen introduced; mandate under plant pest control authority.

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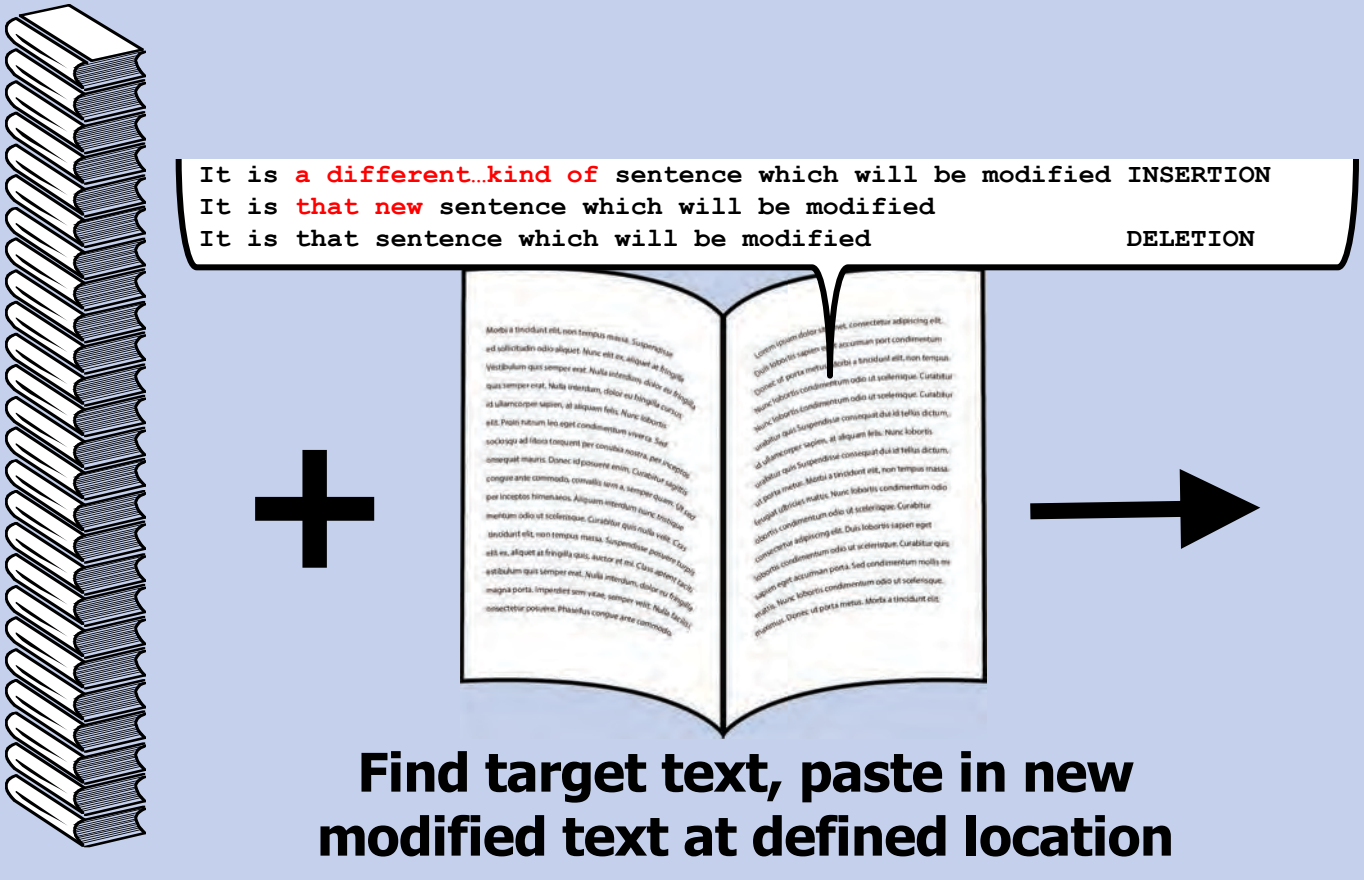
New Genetic Method: Genome Editing-2



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Inserts gene edits specifically in genome

This type of genome editing *may or may not be* GE or GMO, regulated under previous rules and depends on whether it contain viral, Agro, transgenes, etc.

https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-i-regulated

Technology like editing led to calls for revamping U.S. regulation

Genetically engineered crops that fly under the US regulatory radar

To the Editor:

Recently, the US Department of Agriculture

cisgenesis/intragenesis and site-directed nucleases, may be a deliberate strategy for

First step taken on July 2, 2015 by White House Initiative to modernize biotech regulation

approaches or new wrinkles on traditional recombinant DNA techniques in their

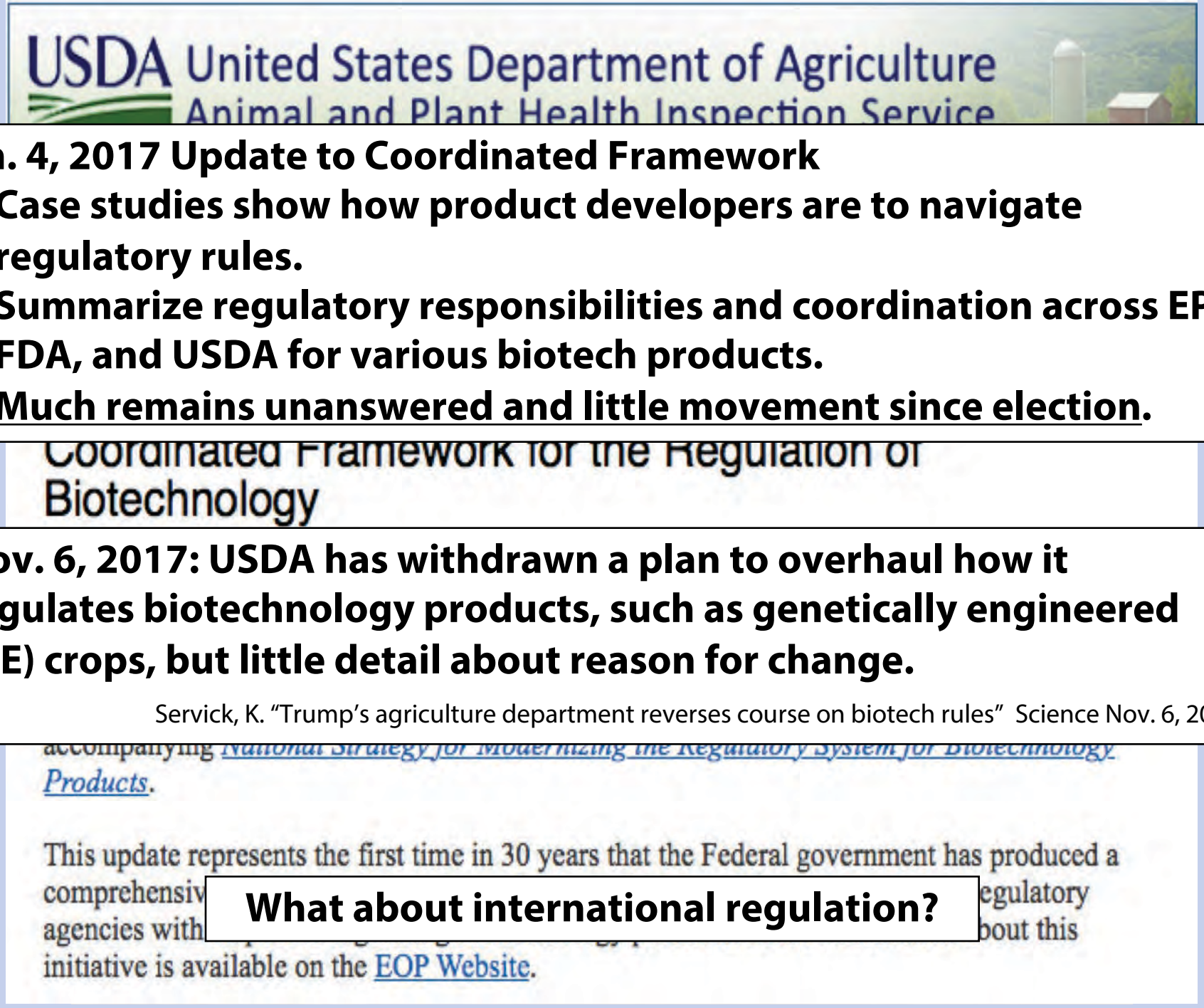
and on the other overregulating GE crops and technologies with proven track records

Charge: Update 1986 Coordinated Framework to clarify roles of 3 agencies to determine what products fall under authority of what agencies. Need to determine how to regulate genome edited products.

institutions or small biotech companies, suggesting that the use of technologies, such as null segregants, novel delivery systems,

scientific knowledge and technologies and, importantly, that allows the participation of small companies and public sector institutions.

Camacho et al. 2014. Nature Biotech. 32:1087-1091



Jan. 4, 2017 Update to Coordinated Framework

- **Case studies show how product developers are to navigate regulatory rules.**
- **Summarize regulatory responsibilities and coordination across EPA, FDA, and USDA for various biotech products.**
- **<u>Much remains unanswered and little movement since election</u>.**

Nov. 6, 2017: USDA has withdrawn a plan to overhaul how it regulates biotechnology products, such as genetically engineered (GE) crops, but little detail about reason for change.

Servick, K. "Trump's agriculture department reverses course on biotech rules" Science Nov. 6, 2017

What about international regulation?

- **Argentina: 2015, genome edited plants fall outside GMO legislation**
- **Canada: considers New Breeding Technology's (like CRISPR) adequately covered by domestic regulation**
- **Sweden: some plants developed thru CRISPR do not fall within EU definition of GMO**
- **Unclear whether EU will agree with Swedish ruling**
- **Greenpe**
  defini **ccur naturally by mating and/or natural recombination"**
- **Jan 2018 Organic Food and Farming Movement (IFOAM) wants to regulate new genetic engineering technologies as GMOs**
- **"Most gene editing techniques should not come under the Europe Union's strict regulatory regime for genetically modified organisms, according to a preliminary legal opinion" Capital Press, Feb. 1, 2018**

So, the "jury is still out"!

Possible trade issue with GE (and edited) varieties

Trade issues occur when engineered (edited?) product is approved in exporting country but not in importing country. Imports can be rejected.

Each country has separate regulations relating to import of GE products: some more liberal than others, causing problems for exporters.