Regulation of Stacked Trait Products

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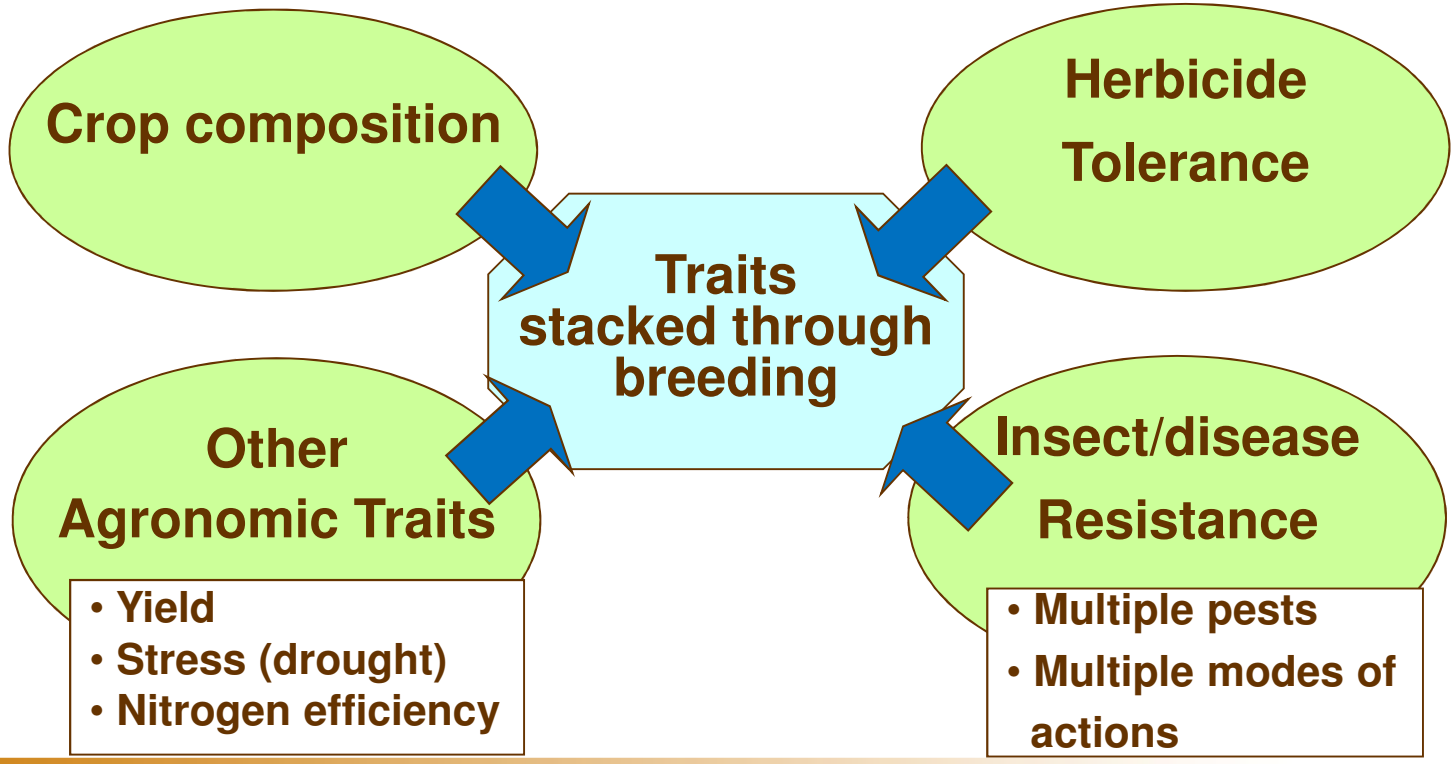
Some thoughts on establishing a “baseline” for discussion

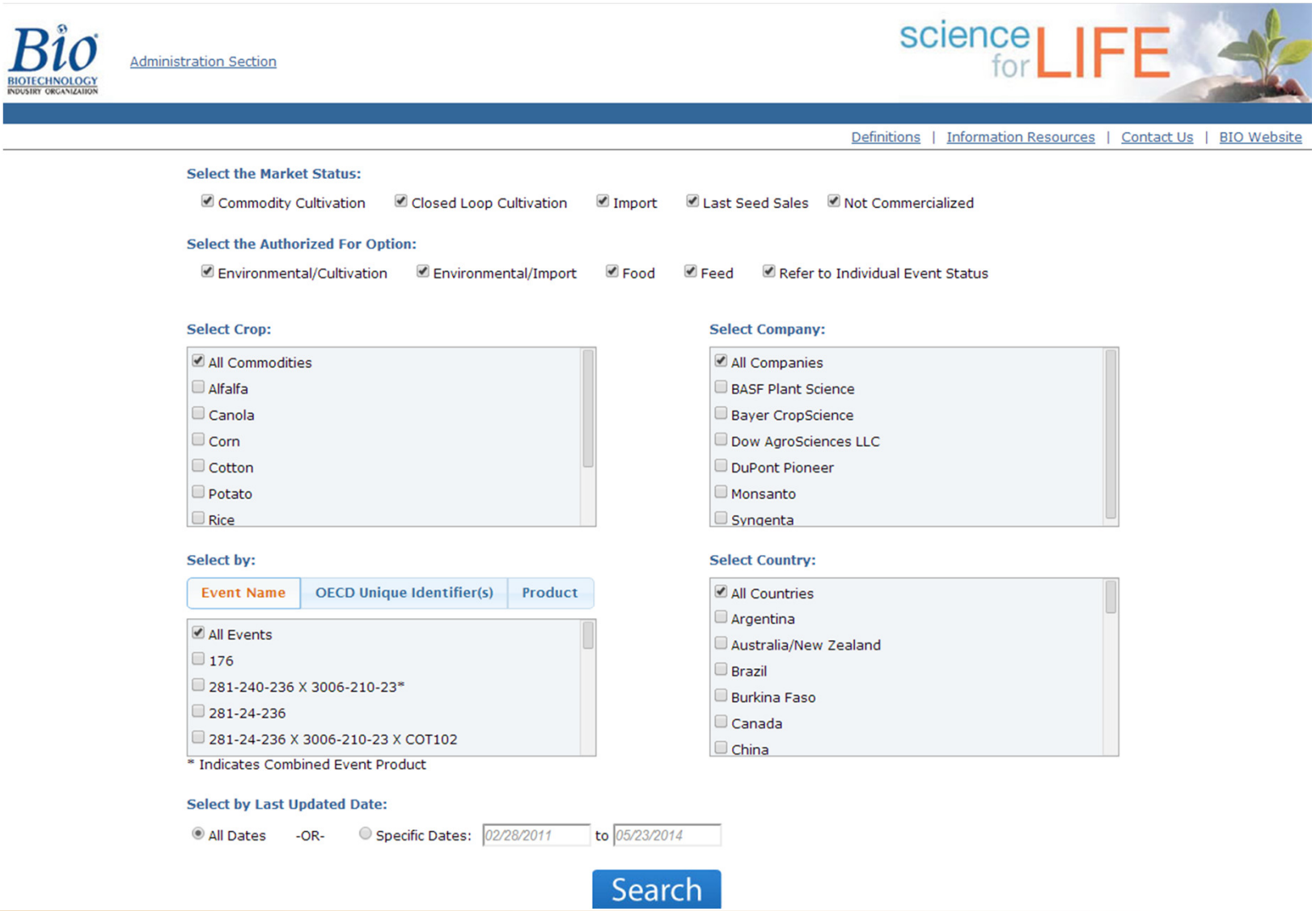
- What stacks of GM events are approved and where?
- A wide range of regulatory oversight
- Is “stacking” of genes a new pursuit in plant breeding?
- Do we have some “familiarity” on which to assess safety?
- Regulating stacks: The “Industry Perspective”

Market demand determines which GM events to combine

- Breeders choose which traits to combine based on their value to customer needs (farmers, consumers)
- The number of breeding stacks is increasing rapidly and encompassing more events due to their value to customers

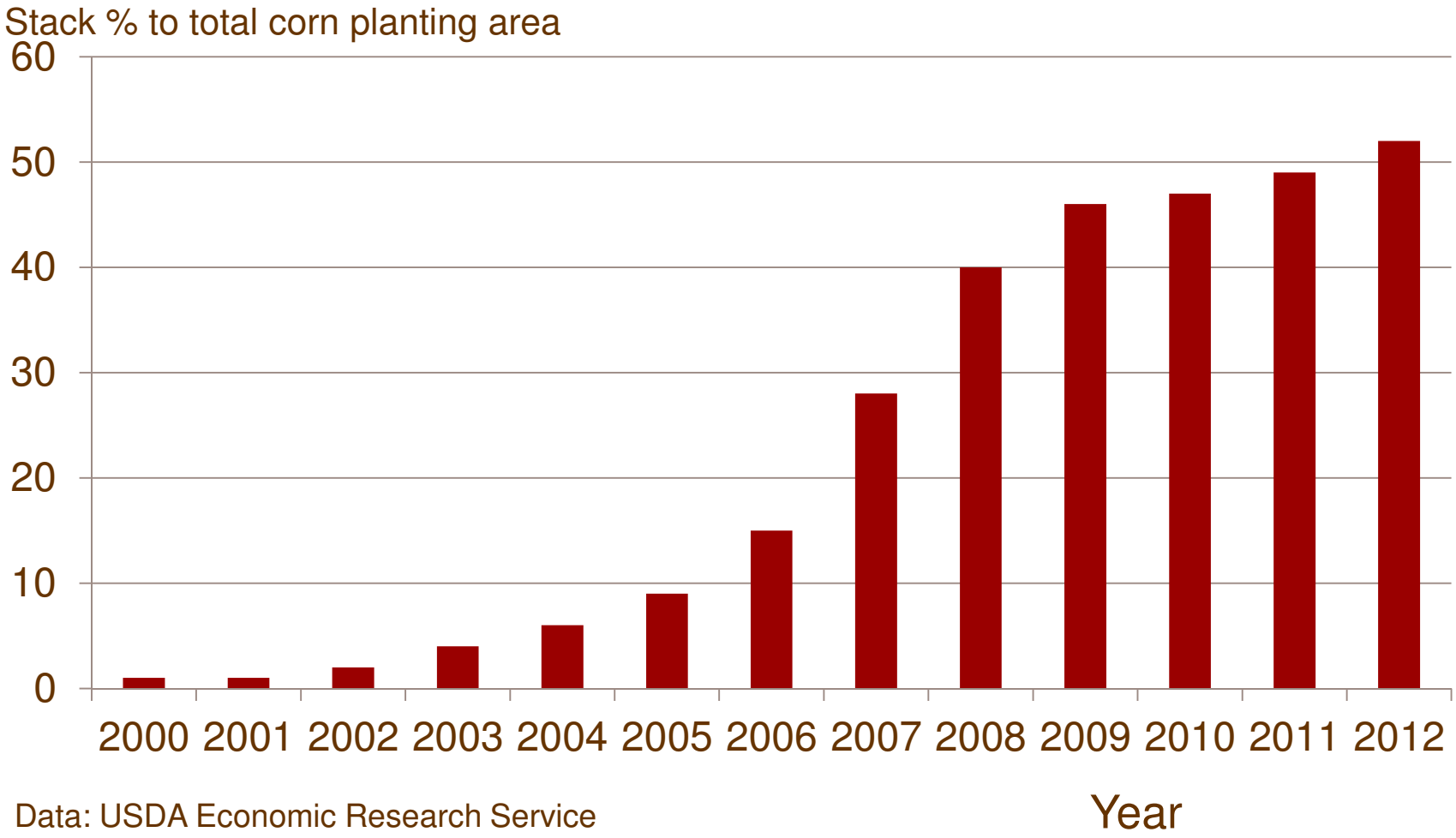


The Bio database provides information on commercialized single and stacked events



Many corn breeding stacks containing 2 - 5 events are already introduced in commerce

In 2012 season, 88% of corn planting area was biotech-derived, and 52% of corn planting area was stacks



Data: USDA Economic Research Service

Global divergence in breeding stack policy

There is some divergence and lack of uniformity in the regulatory process for breeding stacks

Conventional plant breeding has a long history of safe use (HOSU)

2,000 BC — Domestication and Cultivation of chosen crops
19th Century — Selective Cross Breeding
Early 20th Century — Wide-Cross Hybridization
1930s — Cell Culture and Somaclonal Variation
1940s — Embryo Rescue
Mid 20th Century — Mutagensis and Selection
1950s — Polyembryogenesis
1970s — Anther Culture
(1973 microbes) 1983 — Recombinant DNA
1980s — Marker Assisted Selection
1990s — Genomics
Bioinformatics
2000

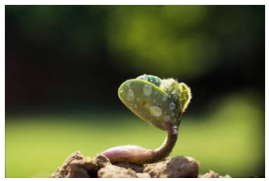
Crops chosen by ancestors

The Plant Breeder

Needs of the Grower

- Performance in different geographies
- Yield
- Consistency in time from planting to harvest
- Standability
- Disease and pest resistances
- No seed shedding, seed sprouting
- Etc.

Desired VARIETY



Needs of the End User

- Competitively priced product
- Exacting quality standards
- Wheat with desired proteins, starches
- Barley with desired proteins
- Maize with desired starches, proteins
- Canola with the desired fatty acids, proteins
- All crops with little or no weed seeds, diseased and damaged harvested crop

Conventional plant breeding has a long history of safe use (HOSU)

- Conventional breeding has been predictably providing safe food and feed products throughout history as well as in the modern era (Pilacinski et al., 2011; FAO-WHO, 2011)
- In more than a century of plant breeding, hundreds of thousands of new varieties have been bred without the emergence of any novel allergens or toxins (Steiner et al., 2013)
- Combining biotech-derived traits through conventional breeding poses no greater risk to food or feed safety than combining non-biotech traits (Kok et al., 2014; Weber et al., 2012; Pilacinski et al., 2011; Raybould et al., 2010; CLI, 2007; WHO, 1995)

The existing safety assessments applied to biotech-derived single events are very robust, comprehensive analyses

The very comprehensive data package for the safety assessment of single event:

- Full Molecular characterization
- Confirmation of the inserted gene segregation according to Mendel Law as well as stability over multiple generations
- Safety of gene product (e.g., protein) including assessment of allergenicity and toxicity
- Assessment of intended and unintended effects through comprehensive composition assessment and on a case by case basis animal feeding studies which take into account potential interactions of the transgene(s) with endogenous plant genes
- For cultivation, both agronomic and phenotypic data are assessed to show that apart from new traits, the plants are substantially equivalent to their non-GM counterparts

Conventional breeding is safe, single events are safe; thus combining singles by breeding is safe

- Conventional breeding has a long history of safe use
- Biotech-derived single events are evaluated in a robust safety assessment
- Breeding stacks are produced by combining previously evaluated (safety affirmed) biotech-derived single events usi ng conventional breeding

Therefore, the safety conclusions based on the single event evaluations are sufficient to inform on the safety of breeding stacks, including all possible sub-combinations of the events

Japan has recently reduced regulation of breeding stack products

- Previous regulation
  - Applicant should submit and obtain approval for every commercialized stack.
  - Approval is granted for the stack only.

- New regulation
  - The approval of higher stack can cover its all lower stacks when all stacked events have no functional interactions each other and no impact to plant metabolism.
  - No data required for herbicide and insect tolerant stack products
  - All possible combinations can be submitted regardless of commercial status.

Summary

- Breeding stacks are developed by conventional breeding which has long history of safe use
- Biotech-derived single events are evaluated in a robust safety assessment
- Need more efficient regulatory process to cover rapidly increasing market demand for breeding combinations of more events
- Propose no separate safety assessment for breeding stacks:
  - Scientifically valid for public defense
  - Less burden on regulatory agencies
  - Facilitates introduction of innovative products to meet agricultural needs - less asynchronous approvals means less possibility for trade disruption

Thank You

Propose only minimal confirmatory data if separate approval for breeding stack is required

- **Confirmatory data to support that the inserted genes in the parental lines are present and functioning as expected when combined in the breeding stack**
  - Trait heritability from parental lines in the breeding stack can be demonstrated at the either one of the following levels but not at the all levels: (1) DNA, (2) Gene product expression, or (3) Trait efficacy
  - **Qualitative expression** of the event products in the article of commerce (grain) provides evidence that the traits are both inherited and functioning in expression as expected
  - In the case of expression below the limit of detection or due to other technical limitations/circumstances, a different assay (e.g., qualitative trait efficacy) can also be used to demonstrate trait heritability and functionality

- **Confirmatory data to support no alteration of other characteristics of parental lines when they are stacked via conventional breeding**
  - Compositional assessment of the article of commerce (grain) of the breeding stack as compared to conventional control
  - Agronomic and phenotypic data can assist in confirming safety of singles remains unchanged when traits are stacked

Agrisure 3122

Bt11 X DAS-59122-7 X MIR604 X TC1507 X GA21

CANADA

Company	Product	Event	OECD Unique Identifier	Crop	Market Status	Authorized For	Updated
Syngenta	Agrisure 3122	Bt11 X DAS-59122-7 X MIR604 X TC1507 X GA21	SYN-BTØ11-1 X DAS-59122-7 X SYN-IR6Ø4-5 X DAS-Ø15Ø7-1 X MON-ØØØ21-9	Corn	Commodity Cultivation	Environmental/Cultivation, Food, Feed	06/12/2013

JAPAN

Company	Product	Event	OECD Unique Identifier	Crop	Market Status	Authorized For	Updated
Syngenta	Agrisure 3122	Bt11 X DAS-59122-7 X MIR604 X TC1507 X GA21	SYN-BTØ11-1 X DAS-59122-7 X SYN-IR6Ø4-5 X DAS-Ø15Ø7-1 X MON-ØØØ21-9	Corn	Import	Environmental/Import, Food	06/12/2013

KOREA

Company	Product	Event	OECD Unique Identifier	Crop	Market Status	Authorized For	Updated
Syngenta	Agrisure 3122	Bt11 X DAS-59122-7 X MIR604 X TC1507 X GA21	SYN-BTØ11-1 X DAS-59122-7 X SYN-IR6Ø4-5 X DAS-Ø15Ø7-1 X MON-ØØØ21-9	Corn	Import	Environmental/Import, Food	06/12/2013

MEXICO

Company	Product	Event	OECD Unique Identifier	Crop	Market Status	Authorized For	Updated
Syngenta	Agrisure 3122	Bt11 X DAS-59122-7 X MIR604 X TC1507 X GA21	SYN-BTØ11-1 X DAS-59122-7 X SYN-IR6Ø4-5 X DAS-Ø15Ø7-1 X MON-ØØØ21-9	Corn	Import	Food, Feed	06/12/2013

PHILIPPINES

Company	Product	Event	OECD Unique Identifier	Crop	Market Status	Authorized For	Updated
Syngenta	Agrisure 3122	Bt11 X DAS-59122-7 X MIR604 X TC1507 X GA21	SYN-BTØ11-1 X DAS-59122-7 X SYN-IR6Ø4-5 X DAS-Ø15Ø7-1 X MON-ØØØ21-9	Corn	Import	Food, Feed	06/12/2013

TAIWAN

Company	Product	Event	OECD Unique Identifier	Crop	Market Status	Authorized For	Updated
Syngenta	Agrisure 3122	Bt11 X DAS-59122-7 X MIR604 X TC1507 X GA21	SYN-BTØ11-1 X DAS-59122-7 X SYN-IR6Ø4-5 X DAS-Ø15Ø7-1 X MON-ØØØ21-9	Corn	Import	Food	06/12/2013

UNITED STATES

Company	Product	Event	OECD Unique Identifier	Crop	Market Status	Authorized For	Updated
Syngenta	Agrisure 3122	Bt11 X DAS-59122-7 X MIR604 X TC1507 X GA21	SYN-BTØ11-1 X DAS-59122-7 X SYN-IR6Ø4-5 X DAS-Ø15Ø7-1 X MON-ØØØ21-9	Corn	Commodity Cultivation	Environmental/Cultivation	06/12/2013

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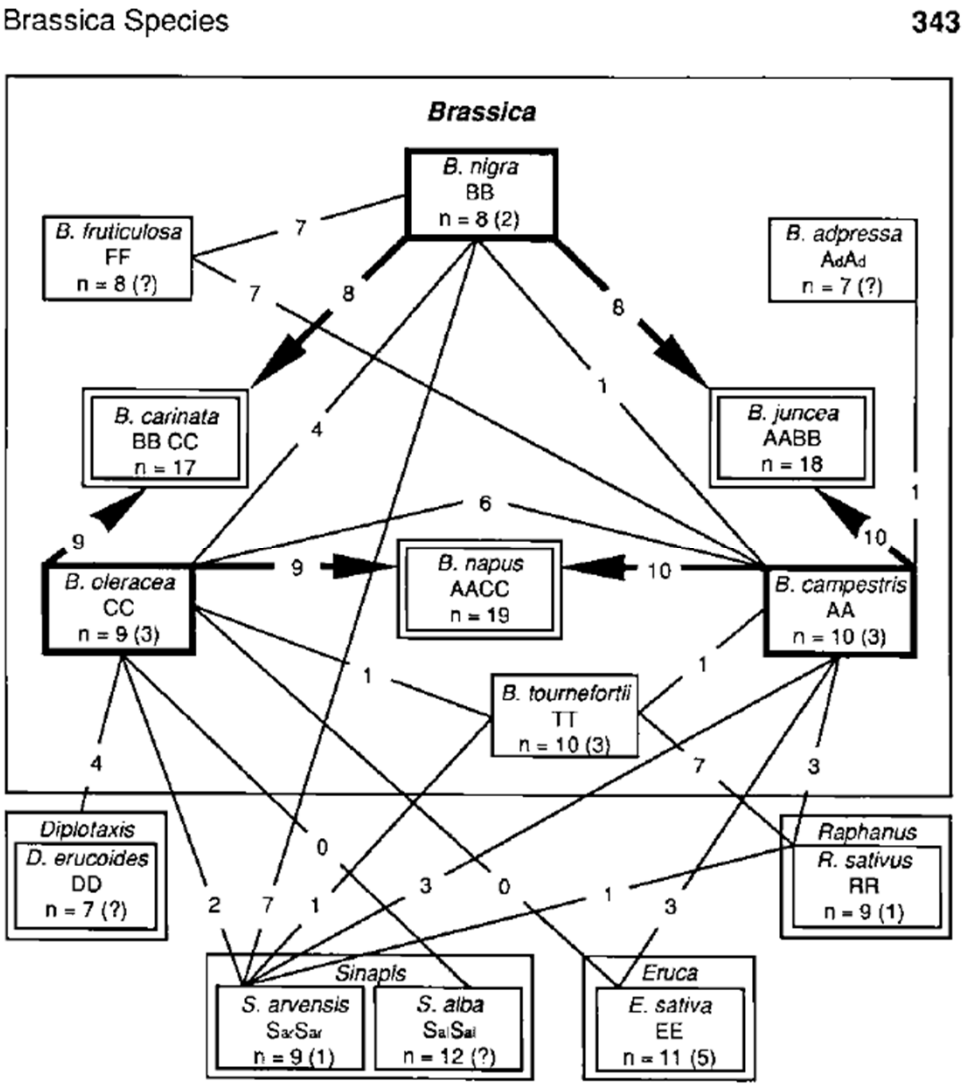
Stacking genes across species – the *Brassicas*



Conventional plant breeding has a long history of safe use (HOSU)

From:

Oil Crops of the World

Their Breeding & Utilization

Ed. Robbelen, Downey R.K. and Ashri A.

McGraw-Hill, 1989