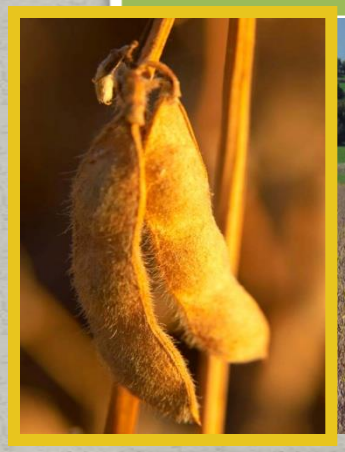
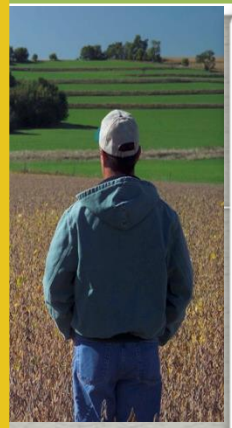
Genetic Editing and Liability for Trade Disruption





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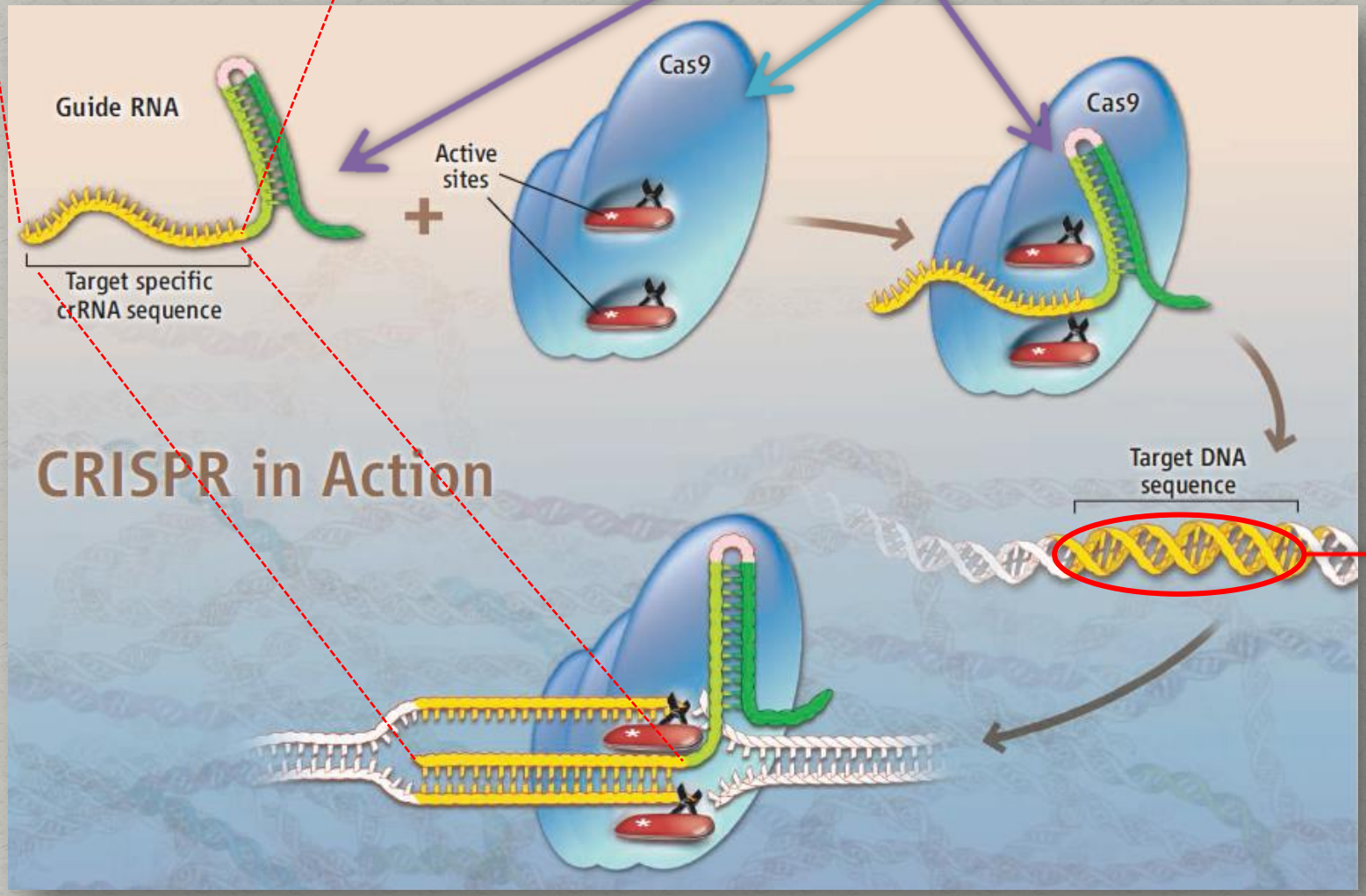
Threats to Genetic Editing in Agriculture

- Patent protection for genetic editing in dispute.
- New traits from new small, start-up companies
- Convention on Biodiversity & Cartagena Protocol on Biosafety – Dec. ‘16 meeting
- Costly approvals, liability are dark clouds
- Expiring patents along with expiring approvals need genetic edited stack -- AgAccord opens door to data compensation.
- U.S. Supreme Court will set boundaries for natural patent and export liability law in next 10-20 years.

DNA needed find target site

Handle locks DNA guide into place

DNA cutting enzyme



DNA sequence to be edited

SCIENCE 341:833-836 23 AUGUST 2013

Genome editing - like editing text?

Difficulty

- CRISPR can delete text (e.g., a couple of nucleotides)
  - E.g., barley, *Brassica oleracea (cabbage, kale etc.)*
  - *Myostatin* deletion in pigs
- Overwrite text
  - E.g., High oleic oil content of soybean goes up (H. Nguyen)
- Insert text
- Zinc-finger nucleases TALENs need “custom proteins”

CRISPR-CAS-9 Patent Litigation

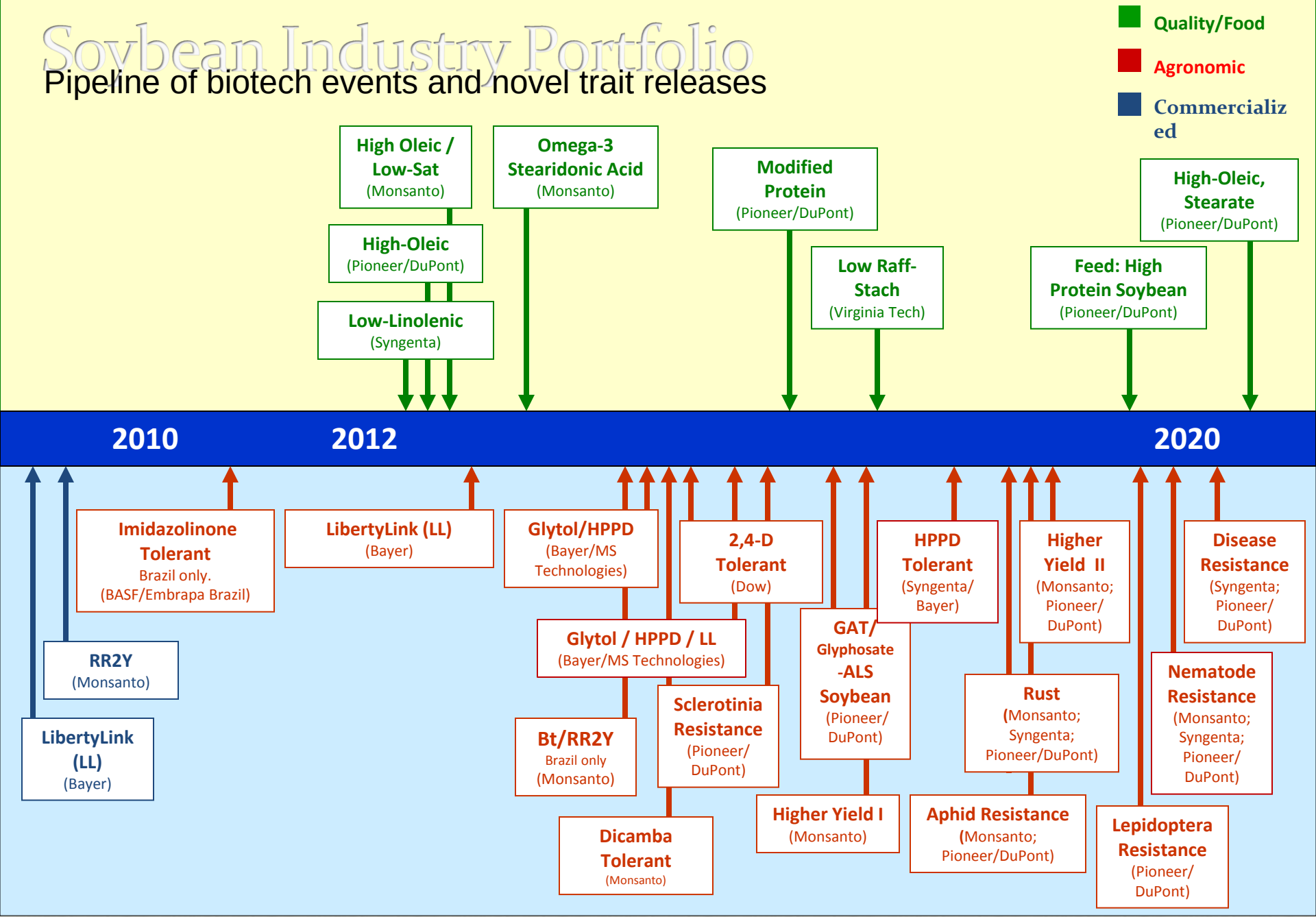
- Clustered Regularly-Interspaced Short Palindromic Repeats/CRISPR associated protein 9
- 2012 U-CA (J. Doudna et al.) denied patent
- 4/14, the USPTO granted Patent No. 8,697,359 to Broad Institute, MIT and Dr. Feng Zhang.
- 1/11/16 US Patent and Trademark Office (USPTO) interference proceeding filed.
- U-CA Regent, Univ. Vienna, & Emmanuelle Charpentier v. Broad Institute, MIT & Harvard
- CRISPR-Cas9 fall under “first to invent” rule.

New Plant Breeding Methods: "Non-GMO"?

- Cartagena-EU regs don't cover these, YET. Only non-recombinant DNA (r-DNA) methods.
- CRISPR "can induce mutations at sites that differ by as many as five nucleotides from the intended target" but it can't it also correct those effects?
- Old r-DNA used viral vectors that irked activists (pleiotropy/off-target effects)
- Many crops used chemical-radiation mutagenesis (huge off-target effects)
- CRISPR could clean up off-target effects of any real concern.

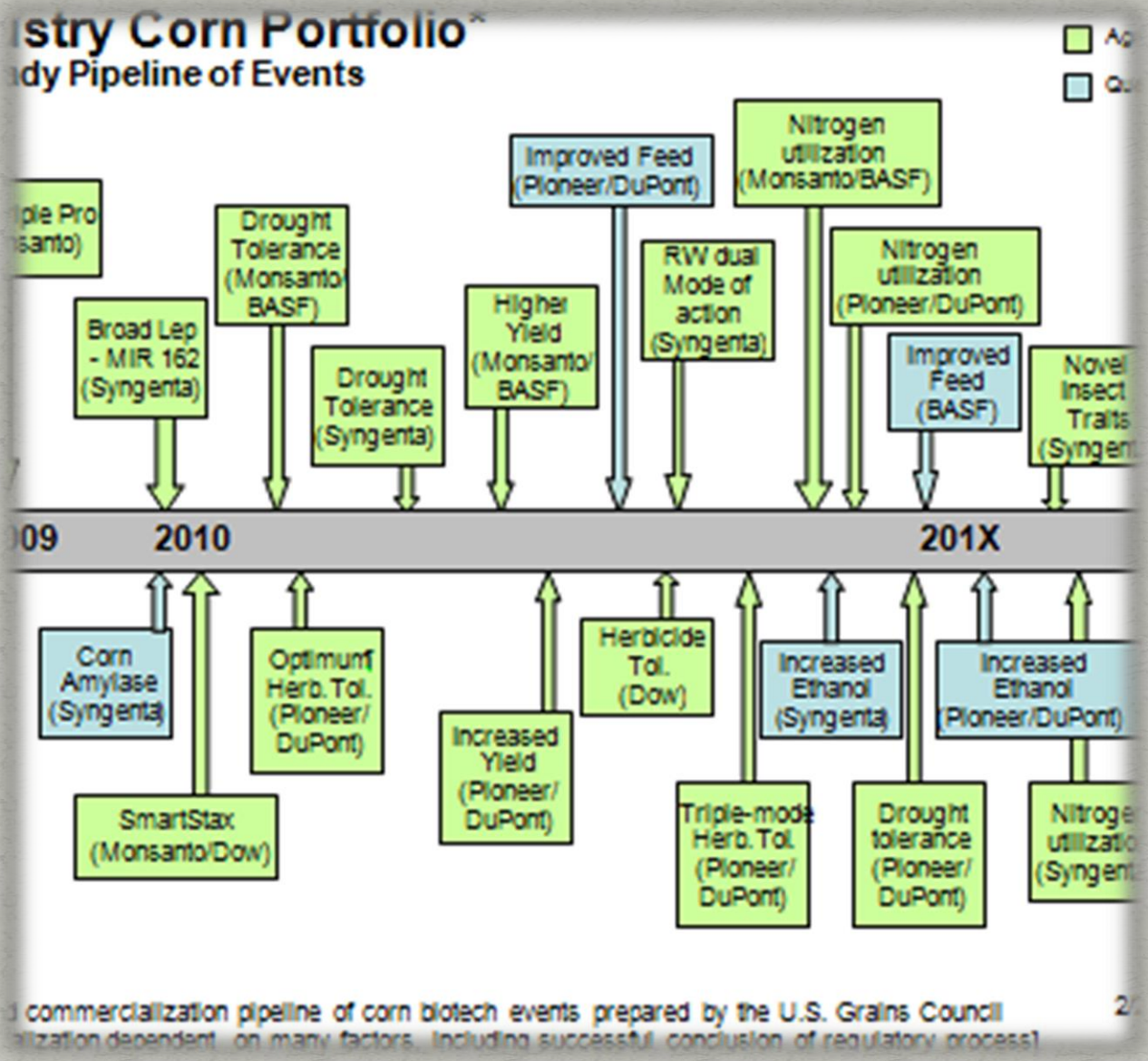
Soybean Industry Portfolio

Pipeline of biotech events and novel trait releases



Source: Pipeline from Industry Sources; prepared by ASA, USSEC, USB. Updated May, 2011

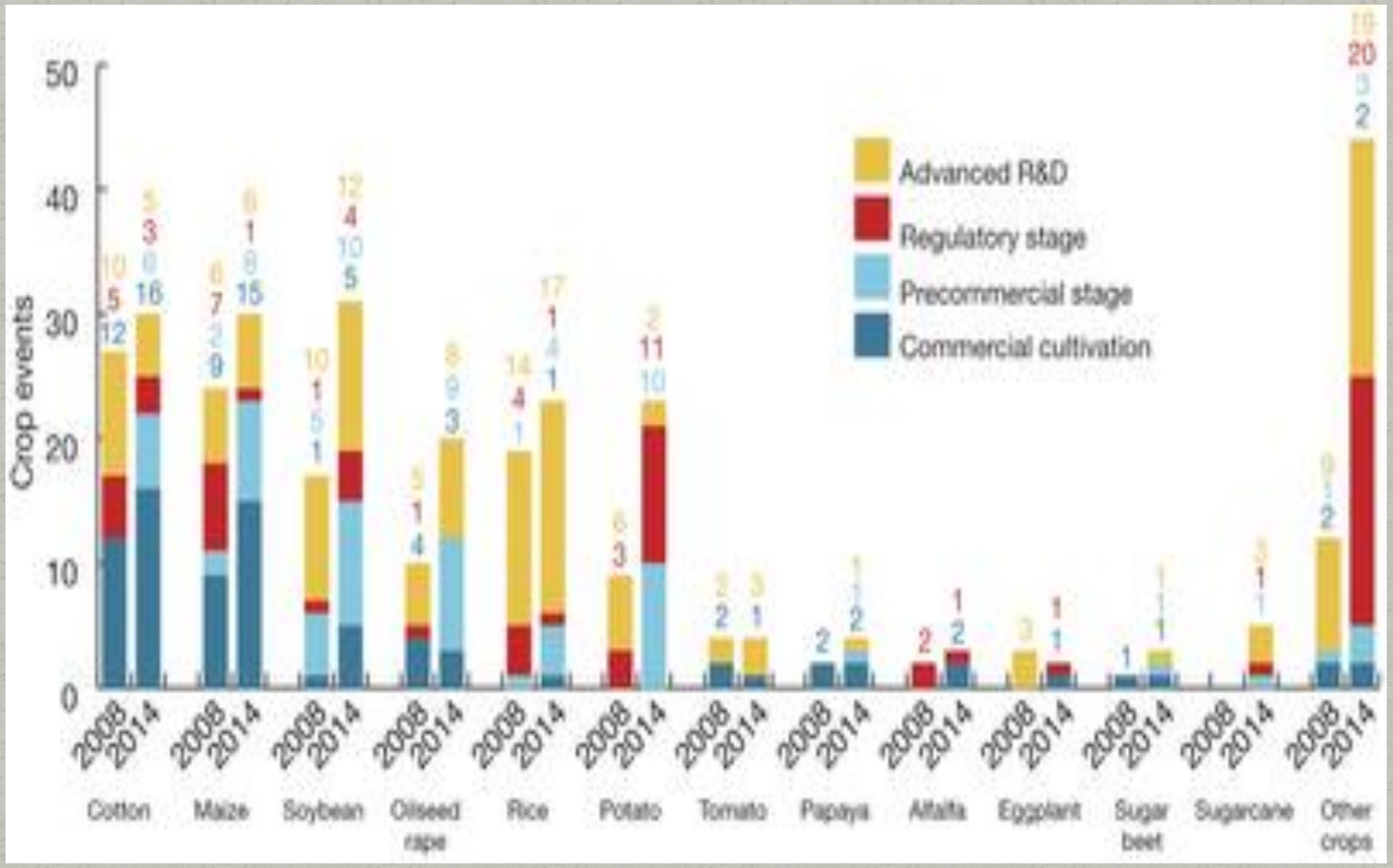
RVSD Biotech Pipeline 050311 V10



BIOTECH CORN & SOYBEAN PIPELINES

- Biotech corn for next 10-15 years?
- Quality & Prod.
- Oil & Meal Improvements
- Industry engaged with "many factors" to consider.
- Corn and Soy have "BRIGHT FUTURE IN MEETING MARKET NEEDS."

Pipelines including earlier stages



CRISPR Corn, Canola and Soybeans

- Dupont “waxy” corn by 2021, wheat too.
- Cibus O-D canola seeking US approval.
- CRISPR soybeans also on market.
- Cartagena Protocol imposes “Precautionary Approach” to regulation, slowing approvals.
- Cartagena also planning to regulate new plant breeding methods – meeting Dec. 2016 (Mexico) starts process of regulation.

CBD and Cartagena Complications

- Convention on Biodiversity gives national sovereignty over genetic resources
  - Compulsory licensing (China soy, Mexico maize)
  - Inhibit research for the next Norman Borlaug.
- Cartagena Protocol imposes Precautionary regulation, slowing approvals.
- Cartagena also planning to regulate new plant breeding methods.

Nations Labeling/Approving GMOS

Biosafety Protocol & Overseas Approval

- "Maintaining authorizations requires scientific, regulatory and political know-how".
- "Traceability" under Biosafety Protocol Article 18.2(a) – proliferating biosafety approval laws.
  - Greenpeace Japan found more stray biotech canola
  - Why Worry/ Just Use IPPC containment.
  - EU testing and tossing at "zero tolerance."
- Nations should recognize familiarity at renewal.
- Genetic editing stacks may need a generic trait.

Overseas Approval & Expiring Patents

- Many nations limit time for approval (China-3, Korea-5, EU-10, etc.).
- Other nations follow their lead? (Biosafety Protocol).
- Stacks may add a new layer of approval, with detection issues that raise costs, errors etc.
- RRS leads way & Industry “AgAccord”

Generic Traits & Trade Disruption

- Approval expiration could cause disruption as "expired" events show up in exports (e.g. RR Soy #1). Industry Ag Accord will prevent this.
- Seed saving actually a relatively minor aspect (growers prefer certified/treated seed).
- Weather loss -- fill in with last years saved soybean non-hybrid seed or U-ARK RRS.
- Seed breeders need to "stack" the free genetic event, or use it in detection in field trials.

Duty to Maintain Overseas Approval?

- Starlink corn – commingling is physical injury
- LL Rice – field trial "illegal" release.
- ASA duty – protect "major markets"
- Syngenta case – duty to foresee "major"
- Post-patent liability – end of life duty to prevent generic crop from causing trade disruption.

Metrics for export markets

- Soy growers 1998 built legal "duties" in soybean stewardship --"***Due Care***" duty saved export markets – negligence to ignore this.
- Does "due care" extend to entire product life cycle include impact of ***generic*** events? (foreseeable?, third party cause this?)
- Liberty Link Rice and Syngenta's litigation raises "economic impact" as nuisance.
- Metrics of Monsanto model post-patent - will BIO & ASTA members follow suit?

Syngenta Case to Extend Liability?

- Does "***Due Care***" duty arise for future export markets that are foreseeable?
- Does "due care" required contained release after sale (e.g., product recalls)?
- Syngenta's misrepresentations re: approval could make bad facts, worse law.
  - While China was asking for a redo of field trial, the CEO is saying March 2012, expect approval.
  - Own employees say "incompetent"

Genetic Editing Liability Prevention

- Seek approval in any foreseeable future export market?
- Participate in industry trade groups and coalitions (e.g., US Biotech Crop Alliance).
- Competent regulatory staff required?
- Can genetic editing companies find the funds to make it to market?

Road Ahead for Genetic Editing in Ag

- Biotech crop pipeline expiring, meeting new DIY era with little genetic editing companies.
- Trade disruption liability can be prevented with stewardship (e.g., AgAccord)
- New plant breeding tools should stack a generic event and keep it on market legally
- Trade agreements can harmonize laws in Cartagena nations (TPP etc.).

Genetic Editing, Meet Generic Traits

- Roundup Ready Soybean (RRS) MON and expired April 2015, LL Soy in 2023.
- Genetic editing stack w/RRS prevents trade disruption liability.
- Sell licensing rights to big seed co. that gets approvals for genetic edited trait, renew generic and approval of stack.

Closing thoughts

- Supreme Court sets “natural” boundary for patents & may set “due care” export standard
- Pipeline of gene-edit biotech crops can succeed
- AgAccord enables stacked events so patent+ renewed approval overseas - could lower the cost of innovative “stacked” crops.
- Cartagena regulation is “dysfunctional” but overseas approval has to be cheaper than billion-dollar litigation payouts.

Thanks!

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