Farm Foundation Round Table - 2019

A Look at Regulating New Technologies

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Biotechnology Innovation Organization (retired)

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A (Backwards) Look at Regulating New (Genetic Modification) Technologies

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Reminders: Genetic Modification of Food

Humans have intentionally changed the genetic makeup of all plants, animals, fungi, microbes used as food and/or used in food processing.

For thousands of years, genetic modification through *human selection* of certain genotypes.

Nature created genetic variation

- Combining existing genes
- Spontaneous mutation

Fruits from Wild Relatives of Crops Prior to GM

Banana

Corn

Tomato

Cucumber

Genetic Modification of Food Crops

Human-driven creation of genetic variation, followed by selection of certain genotypes

1. Combining existing genes
   - 300 years ago, cross breeding – same species
   - 200 years ago, successfully crossed different species
   - 100 years ago, successfully crossed different genera (e.g., bread wheat contains genes from 11 different species in six different genera)

   "unnatural" "wide crosses"

2. Induced mutations to create new genes – 1930's

   Random - chemicals, x-rays

Genetic Modification of Food

Humans creating genetic variation

1. Combining genes – Genetic engineering – 1980's
   (rDNA, transgenics)
   - 1-2 genes, known function, any species
2. Changing existing genes– Gene editing
   - 1-2 genes/nucleotides, known function & location

More specific
More precise
More predictable

Reminders: Genetic Modification of Food

- The function of government regulation is to decrease and/or manage **risks**
- Risk is the *probability* of loss or injury
- Risk = Harm x Likelihood of Exposure
- Government regulation benefits society the most when it balances protection with innovation
- Risks of saying “no” to innovation

Innovation to Solve Problems

Corn variety with new disease

Innovation to Solve Problems

Disease resistant teosinte

Maize variety

Innovation to Solve Problems

Breeding ?

X

Thousands of genes;
functions unknown

or

rDNA ?

Single gene;
known function

rDNA – Recombinant DNA
= “genetic engineering”

Costs of Pre-Market Regulatory Compliance

Breeding ?

X

Thousands of genes;
functions unknown

$ 0

rDNA ?

Single gene;
known function

How did we get here?!!

History of rDNA Regulation

- 1974: A few scientists proposed global moratorium on certain research due to rDNA capability
- 1975: Asilomar conference – 150 participants
- Scientists from 13 countries, lawyers, government officials and representatives from the media
- Developed guidelines for rDNA lab research (Scientist's hope: self-governance)

The DNA Story - James Watson and John Tooze

The Recombinant DNA Controversy - Donald Frederickson

History of rDNA Regulation

- 1976 - NIH Guidelines rDNA Research
- Guidelines relaxed repeatedly (’76 – ’81) as lab experience with rDNA showed no unexpected or unique risks
- 1981/83 – first rDNA animal and plant
- Moving from lab to field and to large-scale manufacturing
- Risks of environmental releases of genetically engineered organisms (GEO’s)?
  - How to assess? Unique or unexpected? Need for new regulations?
  - Predictions/expectations based on science and past experiences

History – Risk assessments of GEO releases

- 1983 – OECD asked an *ad hoc* group of experts from 22 countries to:
  - Create scientific framework for assessing risks of production and use of rDNA organisms (microbes, plants, animals) in agriculture, the environment and industry (i.e., large-scale manufacturing)
- 1986 - Consensus report adopted by OECD member countries
- 1990 - WHO/FAO Expert Consultation reaffirmed 1986 OECD findings and recommendations

Consensus findings of OECD and WHO/FAO experts

- “Industry and agriculture have safely and successfully used conventional methods of genetics on a commercial scale for decades (e.g. cross breeding, mutation, selection)”
- “The use of rDNA techniques does not result in organisms that are inherently less safe than those produced by conventional genetic techniques”
- “Risks associated with rDNA organisms may be assessed in the same way as those associated with conventionally modified organisms.”

OECD – 1986
WHO - 1991

OECD/WHO consensus – Food safety assessment

- Foods developed, prepared and used in traditional ways are considered safe.
- Because rDNA does not inherently lead to GEO's that are less safe, assess safety by determining if GEO is *substantially equivalent* to organisms developed by conventional means.
- Comparative, familiarity-based approach to assessing risks

OECD - 1993
WHO - 1996

Summary – 1980's Scientific consensus on risks of GEOs

- No evidence of unique risks of rDNA or in transfer of genes between unrelated species.
- Risks of GEOs are based on characteristics of GEO and not on method used to produce it.
- Risks of GEOs are same in kind as non-GEOs with similar traits produced by traditional genetic methods.
- Therefore, in determining potential for harm, look to non-GEOs with traits similar to the GEO.

1980's Global Scientific Consensus on GEO Risks

Risk GEOs = Risks non-GEOs

Risks based on nature of product, not process

- OECD and WHO/FAO Expert Panels
- U.S. National Academy of Sciences
- International Council of Scientific Unions
- NATO Workshop Proceedings
- Ecological Society America
- American Medical Association
- Office Technology Assessment (US Congress)
- Environmental Defense Fund
- Audubon Society

Regulatory policy recommendations – OECD report

OECD *ad hoc* group of experts (1983) asked to review existing or planned legislation and regulations on rDNA organisms

Findings:

"There is a broad array of existing legislation relating to health, safety and environmental protection, which could be applied to rDNA organisms. In addition, specific provisions for the application of rDNA techniques can be found in the form voluntary guidelines or recommendations."

Recommendation:

" There is no scientific basis for specific legislation for the use of rDNA techniques and applications."

OECD – 1986

Regulatory policy recommendations – OECD report

- If modified crop is determined to be substantially equivalent to existing crop, then further safety or nutritional concerns are expected to be non-existent or insignificant.
- Once substantial equivalence has been established, such crops should be treated in the same manner as their conventional counterparts.

OECD 1993

OECD 1986 report and “case-by-case” review

- Comparative, familiarity-based approach to safety assessments implies case-by-case review.
- “Case-by-case means an individual review of a proposal against assessment criteria which are relevant to the particular proposal; this is ***not*** intended to imply that every case will require review by a national or other authority since various classes of proposals may be excluded.”

OECD – 1986

Risk assessment – Environmental releases of GEOs

- International consensus approach to assessing risks of releases of rDNA organisms (GEO's) was established in mid-1980's.
  - Based on science-based expectations/predictions and real world experiences with organisms modified by other genetic techniques
- 35 years of scientific research and real world experiences with GEOs have confirmed the validity of approach and recommendations proposed in 1980's.

Consensus findings – Real world experiences

- “Industry and agriculture have safely and successfully used conventional methods of genetics on a commercial scale for decades (e.g. cross breeding, mutation, selection)”
- Foods developed, prepared and used in traditional ways are considered safe.

OECD – 1986
WHO - 1991

Real world experiences – Food safety risks

New, genetically modified crop varieties and animal breeds released repeatedly in the past centuries

- Thousands of new crop varieties released every year
- No instance of harm to health or environment due to conventional methods of genetic modification

International Food Biotechnology Council. 1990. Biotechnologies and food. Assuring the safety of foods produced by genetic modification. *Regulatory Toxicology and Pharmacology.* 12:SI - SI96
http://ilsirf.org/wp-content/uploads/sites/5/2016/06/01_1990RegToxPharm-CSAFF.pdf

1992 FDA Policy – *All* New Plant Varieties

"Any genetic modification technique has the potential to alter the composition of food in a manner related to food safety, although, based on experience, the likelihood of a safety hazard is typically very low … because producers of new foods have an obligation to ensure that the foods they offer to consumers are safe and in compliance with applicable legal requirements."

Therefore, "plant breeders, using well established practices have successfully identified and eliminated plants that exhibit unexpected, adverse traits prior to commercial use."

Familiarity-based risk assessment

- Using what we already know to assess risks
- Risk = Harm x Likelihood of exposure

  - Plant breeder's knowledge of and **ex**perience with crop
  - Scientific literature on the crop and its uses
- No harm to health or the environment (n = trillions)
- Risk = Zero harm x Likelihood of exposure
- The function of government regulation is to decrease and/or manage **risks** ……

Costs of Pre-Market Regulatory Compliance

Breeding ?

X

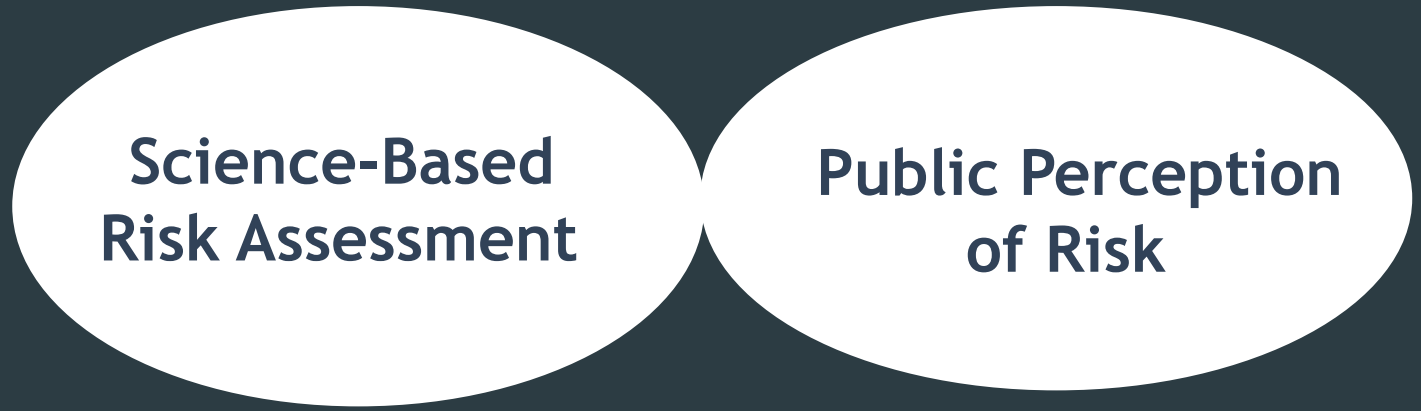
Thousands of genes;
functions unknown

$ 0

rDNA ?

Single gene;
known function

Risk and Regulation



- Regulatory policy is shaped by:
- Science-based risk
- Public perception of risk

Risk and regulation of rDNA organisms

Creation of the U.S. regulatory system for GEOs

- Was an attempt to reassure the public
- Had nothing to do with scientific consensus on risks

“ The goal in developing the ‘Coordinated Framework’ was to explain to the American public that, for questions involving the products of biotechnology’ (more specifically, organisms derived from recombinant-DNA technology), human health and the health of the environment were of paramount concern and were adequately protected.

- David Kingsbury

U.S. 1992 “Scope” Policy Statement

How U.S. agencies would regulate GEOs

- Discretionary oversight based on risk:
  “…oversight shall be exercised only where risk …is unreasonable, i.e., when value of risk reduction obtained by oversight is greater than the cost imposed.”

1992 “Scope” Policy Statement

How agencies would regulate GEOs

- Oversight based on product, not process:

  “should not turn on the fact that an organism has been modified by a particular process or technique.”

U.S. Regulatory System – Food Crops

All food crops in U.S. are subject to regulation – Post Market Oversight

Pre-market regulatory review and approval was added to post-market oversight for GE crops

Pre-market oversight is the norm for new products expected to pose hazards

- Pharmaceuticals
- Chemical Pesticides

The Problem with Pre-Market Oversight

The more we learn about biology, the more questions regulators ask

Want to Know vs. Need to Know
- increases data requirements/costs
- increases uncertainty

The pre-market approval “dance” between developers and regulators

EPA Quotes on Risks and Benefits

"…**no documented harm to human health or the environment** has been confirmed for any of the Bt crop varieties." 1999

"EPA believes that available scientific data and information indicates that **cultivation of Bt crops has a positive ecological effect, when compared with the most likely alternatives.**"1999

" The US EPA's analysis of Bt crops finds that they pose no significant risk to the environment or to human health." 2003

EPA Data Requirements Bt Crops 1995 – 2011

	Number of Studies to Assess Risks		
Data Category	1995	2008	2011 Proposal
Product Characterization	7	10	1 new; 5 - increase scope
Human Health	1	4	4 new; 1 - increase scope
Non Target Organisms	4	8	4 new; 6 – increase scope
Environmental Fate	1	1	4 new; 1 – increase scope

Opportunity costs

U.S. Field Trials of GE Plants

	Fruits/Vegs	Commodity
1992	44%	53%
2002	15%	83%

Opportunity costs

Requests for Commercial Approvals

	Type of Traits	
	Product Quality	Agronomic
93 – 96	45%	53%
97 – 99	24%	73%
00 – 04	5%	93%

Opportunity Costs

Public sector researchers and small companies cannot afford to develop products

Multinational corporations are also affected

What Could Have Been in GE Crops

- Potato – Amaranth protein – Most essential amino acids
- Soybean – Increased lysine 5 times
- Grains – Increased amount and availability of vitamins & iron
- Fruits and Vegetables – Stay fresh longer
- Soybean – Designer fatty acid profiles (increase monounsaturated; eliminate trans fatty acids; omega 3's)
- Fruits/grain – Nutraceuticals found in vegetables – lycopene, glucosinolates, lutein, isoflavonoids, saponins
- Peanuts, etc.- Low allergenicity
- Wheat – Low gluten
- ……

Genetic Engineering Could Have Provided

- Mastitis resistance in many livestock breeds (2001 - 08)
- Bacterial resistance in livestock/fish (1991, 2002, 2004)
- BSE (“mad cow”) resistant cattle/sheep (2001 & ‘07)
- Poultry incapable of transmitting bird flu (2010)
- Swine with less fat; lower cholesterol (1994; 1999)
- Omega-3 swine (2006)
- Swine that excrete less phosphorous (2001)

Thank You!