Liability Prevention and Intergenerational Genomic or Epigenetic Harm

Thomas P. Redick

GEEC, LLC

Clayton, MO

www.geeclaw.com

Governance of Emerging Technologies Conference

May 28, 2015

Overview of Presentation

- Biotech animals, microbes and crops via new epigenetics breeding (CRISPR, TALENS, oligo-directed etc.)
- Foods quietly (?) improved outside U.S. regulatory approval (overseas approval?)
- Our liability system is reactive and overprotective , compensating harm that falls outside of regulation.
- Preventing liability requires advanced “foreseeing” of potential harm.

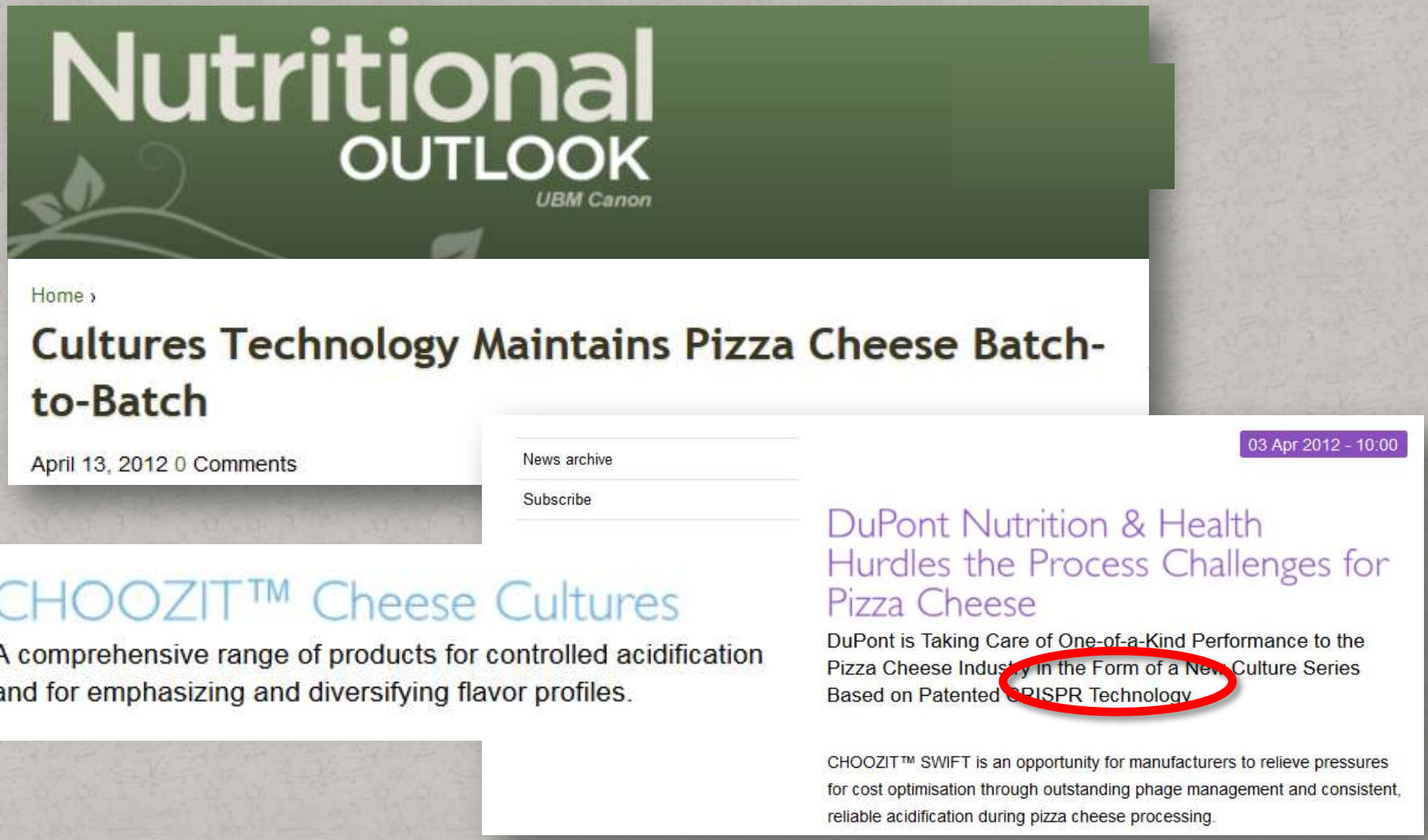
Basic principles of liability risk

- Epigenetics links to litigation risks of DNA & immune/endocrine "harm"
- New breeding methods reduce risks
- We can lower the regulatory barriers only if we show advanced industry liability prevention is possible.
- Liability case studies point toward a future where we use science to foresee and prevent potential harm.

Overview – GMO liability history

- Generations & endocrine harm -DES
- L-tryptophan "GMO" personal injury
  - Genetic alternative cause - defense
  - Genetic susceptibility – offense
- DNA cross-links & medical monitoring – Erin Brockovich fans fear of cancer
- Gene editing duty to warn?

Genetic Editing will transform our food supply in this century



Nutritional OUTLOOK
UBM Canon

Home ›

Cultures Technology Maintains Pizza Cheese Batch-to-Batch

April 13, 2012 0 Comments

News archive

Subscribe

03 Apr 2012 - 10:00

DuPont Nutrition & Health Hurdles the Process Challenges for Pizza Cheese

DuPont is Taking Care of One-of-a-Kind Performance to the Pizza Cheese Industry in the Form of a New Culture Series Based on Patented CRISPR Technology

CHOOZIT™ SWIFT is an opportunity for manufacturers to relieve pressures for cost optimisation through outstanding phage management and consistent, reliable acidification during pizza cheese processing.

CHOOZIT™ Cheese Cultures

A comprehensive range of products for controlled acidification and for emphasizing and diversifying flavor profiles.

Beyond cheese:

BREAKTHROUGH OF THE YEAR

Science 20 December 2013:
Vol. 342 no. 6165 pp. 1434-1435
DOI: 10.1126/science.342.6165.1434-a

NEWS

Genetic Microsurgery for the Masses

A gene-editing technique called CRISPR touched off an explosion of research in 2013, leading *Science*'s editors to name it a runner-up for the 2013 Breakthrough of the Year.

- 1770 literature citations since 2012
- We can rewrite the genome of anything with a gene – let's start with food, its less controversial?

Plants • Medicine • Animals

Scientific Correspondence

Efficient Gene Editing in Tomato in the First Generation Using the Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-Associated9 System[1]

Christopher Brooks, Vladimir Nekrasov*, Zacha
Cold Spring Harbor Laboratory, Cold Spring Ha
Norwich Research Park, Norwich NR4 7UH, Unit
Science, Ithaca, New York 14853 (J.V.E.)

RNA-Guided Human Genome Engineering via Cas9

Prashant Mali,[1]* Luhan Yang,[1,3]* Kevin M. Esvelt,[2] John Aach,[1] Marc Guell,[1] James E. DiCarlo,[4] Julie E. Norville,[1] George M. Church[1,2]†

Bacteria and archaea have evolved adaptive immune defenses, termed clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) systems, that use short

S1C; see supplementary text S1 for a detailed discussion).

To test the functionality of our implementation for genome engineering, we developed a green fluorescent protein (GFP) reporter assay (Fig. 1B) in human embryonic kidney HEK 293T cells similar to one previously described (*10*). Specifically, we established a stable cell line bearing a genomically integrated GFP coding sequence disrupted by the insertion of a stop codon and a 68-bp genomic fragment from the AAVS1 locus enders the expressed protein fragment non- escent. Homologous recombination (HR) an appropriate repair donor can restore the l GFP sequence, which enabled us to quan- he resulting GFP⁺ cells by flow-activated orting (FACS).

test the efficiency of our system at stim- g HR, we constructed two gRNAs, T1 and at target the intervening AAVS1 fragment 1B) and compared their activity to that of a usly described TAL effector nuclease het- mer (TALEN) targeting the same region

BIOLOGY OF REPRODUCTION (2014) **91**(3):79, 1–3
Published online before print 6 August 2014.
DOI 10.1095/biolreprod.114.123935

Commentary

CRISPR Bacon: A Sizzling Technique to Generate Genetically Engineered Pigs

Franco J. DeMayo[1] and Thomas E. Spencer,[2] *Editors-in-Chief, Biology of Reproduction*

[1]*Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, Texas*
[2]*Department of Animal Sciences and Center for Reproductive Biology, Washington State University, Pullman, Washington*

Regulation Evolving for new technology

- Regulatory attitudes of various nations are evolving – likely that products using epigenetic methods will be regulated in some markets (Canada, EU, Japan etc.).
- Regulators may realize plant and animal breeding is evolving into precise tool.
- As only tool for eliminating defects in DNA and epigenetics.

IARC Cancer Probability -- Glyphosate

- Duty to warn changing as epigenetics supports "probable cancer" label?
- Are they reading Drs. Seneff/Samsel?
  - "exogenous semiotic entropy"
  - Epigenetic effects (sulfate transport) caused by glyphosate?
- "Pseudoscience poster child" who spent $10,816.00 to publish papers

DES Case Breaks Ground, Set Limits

- Cannot Identify Manufacturer?
  - "Market Share" Liability for drug
  - Mfr. must prove it did not cause plaintiff's harm or share damages
  - California adopts novel theory in DES
  - Federal court -- 13 of 15 states follow?
- Why? Intergenerational Endocrine harm
  - Daughters vaginal cancer via *in utero*
  - Grand-daughters could not sue

1989 L-Tryptophan Recall & Ensuing Litigation

- FDA "Generally Recognized as Safe"
- Sold GM bacterial fermentation process as "natural" drug using amino acid intended for animal feed.
- New Mexico case: "eosinophilia" – overactive white blood cells.
- FDA and CDC act, ban/recall L-t.
- Consumers sued Showa Denko, WSJ reported $3 billion paid (and rising)

L-Tryptophan Caused by "GMO" bacterium?

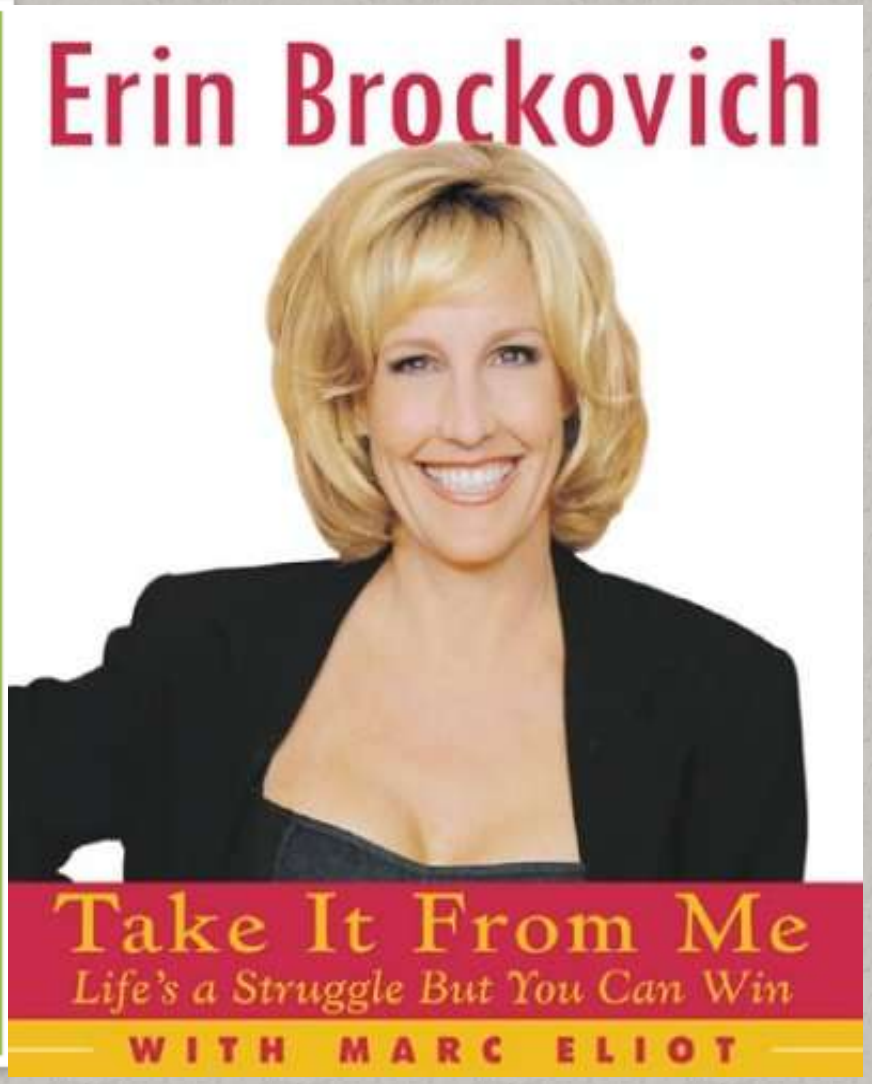
- Impurities in bad batches are more likely to have caused disease - Negligent failure to use filters alleged.
- 37 deaths and over 1500 injured.
- 1996 -- $1.05 million affirmed on appeal.
- Genetic alternative cause - defense
- Genetic susceptibility – offense

DES and L-Tryptophan Lessons Learned

- U.S Regulatory oversight won't prevent liability if they miss a risk.
  - Deep Pockets attract litigation.
  - Tracing back allows plaintiffs to prove link.
- "GMO" process has a target painted on it.
  - 20 years later, Taiwan assuming GE cause?
  - Activist: "Showa Denko's genetically engineered bacteria could have been responsible for the EMS epidemic."

ENTER ERIN BROCKOVICH, FANNING DNA CROSS-LINK "FEAR OF CANCER"

- Cancer-phobia can be based on mere 'doubling" of the risk of cancer under CA Law
- Has to be "malice" and PGE had ample quantities.
- Lessons – be open and transparent, invest in safer tech even if costly in short term.
- Erin looking for the next big case.



Starlink Corn Recall & Allergy Litigation

- Growers sued Aventis for economic loss for "physical injury" of commingling in stream of commerce.
- Consumers claimed, could not prove, allergy
- Under $1 billion paid in settlement?
  - Reports of settlements under $1 bil.
  - Unreported recall cost of food companies might put this cost over $1 billion.
  - $2 billion shareholder loss
- Export markets rejecting U.S. corn – will epigenetic crops face similar barriers?

Legal Barriers to Epigenetic Liability

- Statutes of Limitations / Repose
  - Limitation – bring suit within N years, unless you have a good excuse (DES got states – NY – to extend with one-year window)
  - Repose – time runs from event, not injury
- Product Identification
  - Tracing diseases to epigenetic injury
  - Market share to be allowed?
- Medical Causation and Alternative cause
  - Reproducible, peer-reviewed.
  - Long latency periods before disease.

Conclusion: Industry Must Foresee

- Regulatory review should never be assumed to catch every foreseeable adverse event in advance.
- Post –market monitoring required
- Industry must collect data on possible adverse events has to include epigenetic impacts.
- Law may evolve further to capture subtle subclinical harm and award medical monitoring damages.

My Books on Liability Law

- Lewis Bass and Thomas P. Redick, Products Liability: Design and Manufacturing Defects, 2014-2015 ed. (The West Group, 2015). www.legalsolutions.thomsonreuters.com

- Thomas P. Redick, Stuart Smyth, Drew Kershen and Bryan Endres, "Innovation and Liability in Biotechnology: Transnational and Comparative Perspectives". (Edward Elgar press) (2010) http://www.amazon.com/Innovation-Liability-Biotechnology-Transnational-Perspectives/dp/1847206646

Thanks!

tpr@geeclaw.com