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Perceptions of Validity: How Knowledge is Created, Transformed and Used in Bio-Agricultural Technology Safety Testing for the Development of Government Policies and Regulations

Jennifer Josephs
Nova Southeastern University, jen.j.josephs@gmail.com

Perceptions of Validity:
How Knowledge is Created, Transformed and Used in Bio-Agricultural Technology Safety Testing for the Development of Government Policies and Regulations

by

Jennifer Joy Josephs

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Ismael Muvingi, Ph.D.
Committee Chair

Robin Cooper, Ph.D.
Committee Member

Elaina Bastidas, Ph.D.
Committee Member

February 10th 2017
Date of Final Approval

Ismael Muvingi, Ph.D.
Committee Chair

Dedication

This is dedicated to my father—my mentor, my friend, my teacher, my dad.

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Thank you, Mom, for teaching me how to appreciate the little things, encouraging me to explore and showing me how to come home. Thank you, Dad, for teaching me to reflect deeply and showing me how to engage as a conscientious citizen. Your lessons have helped me experience and understand the world intricately and broadly. Your spirits have guided me, encouraged me and helped to keep me grounded.

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List of Acronyms

AMPA	Aminomethylphosphonic acid
APHIS	Animal and Plant Health Inspection Service
BfR	Bundesinstitut für Risikobewertung (Germany's Federal Institute for Risk Assessment)
DDT	dichlorodiphenyltrichloroethane
EC	European Commission
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FDA	Food and Drug Administration
GAO	Government Accountability Office
GE	Genetically Engineered
GMO	Genetically Modified Organism
GPO	(U.S.) Government Publishing Office
GRACE	GMO Risk Assessment and Communication of Evidence
G-TWYST	Genetically modified plants Two-Year Safety Testing
IARC	International Agency for Research on Cancer
LA	Lead Arsenate
OECD	Organization for Economic Cooperation and Development
OMB	Office of Management and Budget

OSTP	Office of Science and Technology Policy (Executive Branch)
RED	Reregistration Eligibility Decision
TSCA	Toxic Substances Control Act
US	United States
USDA	United States Department of Agriculture
USDA-ARS	United States Department of Agriculture – Agricultural Research Service
USDA-ERS	United States Department of Agriculture – Economic Research Service
WHO	World Health Organization

Abstract

This is a case study dissertation to research the socio-political conflict surrounding Gilles Eric Séralini's et al (2012) research on the toxicity of Monsanto's NK603 line of corn and the herbicide Roundup. The study analyzes this conflict as a system of interconnected and often conflicting interests, assumptions and ideologies about how knowledge is created and transformed from the research stage to the policy implementation stage. The goal of this study is to: 1.) analyze critical surface level and underlying factors that contribute to the conflict; 2.) analyze systemic processes between national and international researchers, private interests and government policymakers in developing and implementing research protocols, policies and regulations pertaining (but not limited) to Monsanto's NK603 corn and Roundup; 3.) identify potential patterns of knowledge transformation from the research stage to policy implementation. The theoretical approach used in this study considers social construction, critical theory and Kuhn's theory of scientific revolution. In utilizing case study methodology, this study incorporates internal analysis of Séralini's case with a basic comparative analysis of DDT and lead policy processes and knowledge transformation, using mainly secondary data sources supplemented with primary interview material from two select researchers using purposive sampling. By conducting this research, it is hoped that this study reveals a better understanding of the complex interconnected systems that help create and transform food safety policies and the science that supports and/or transforms them.

Chapter 1: Introduction

Background

The Basics

It might be helpful to first get a basic understanding (a much more in-depth conversation follows throughout the text) of how crops are regulated within the U.S. For the last several decades, U.S. conventional crop regulation has been divided between the USDA, the FDA and the EPA. The USDA determines the hazardous potential of a crop to ensure that crops, when they are approved by the USDA (e.g. new crop varieties derived from hybridization), do not pose a threat to the agricultural system (e.g. beneficial plants and insects) and surrounding environment. The EPA ensures that the pesticides used in crop production are safe for human (and animal) consumption by analyzing toxicity studies and setting pesticide residue levels based on their assessment of those studies. Those pesticide residue levels are then tested, to some extent, by the USDA and the FDA. The main function of the FDA, in terms of food safety, is to ensure that after a crop (grown for human consumption) is harvested and/or manufactured for commercial sale the end product is free from hazardous substances that could threaten human health—including checking for pesticide residue level compliance. These agencies do not simply test what others give to them, but they also conduct their own research, expanding their understanding and capacity to address current and potential health hazards that might stem from the U.S. agricultural production and consumption system.

United States Department of Agriculture

The safety of the U.S. agricultural system could be considered a source of pride for farmers, consumers, and policymakers alike. Part of American cultural heritage prides itself on "pulling oneself up by one's own bootstraps" and it ties in well with the bold, courageous and innovative efforts it took to develop what was once considered by European settlers as a "wild and hostile" land. Agriculture has been central to U.S. settlement, development and prosperity as it provides a basis, literally, for growth. The United States Department of Agriculture (USDA) has been supporting U.S. agricultural development for over 150 years (first established in 1862 when Abraham Lincoln signed into law what he dubbed "the people's department") providing public research and resources that promoted plant and soil sciences to improve and increase U.S. crop viability and production. A multitude of USDA public programs have helped grow and distribute our nation's food supply to not only the general population, but also addressing the food and nutritional needs of the poor. Part of the efforts in increasing yield and decreasing production costs of the U.S. agricultural system was built on an increasing dependence on chemical inputs (e.g. pesticides and fertilizers), but although U.S. production rates were impressive, the negative consequences (public and environmental health) of many of the chemicals used in the past (e.g. lead arsenate and DDT) undoubtedly made for a more inviting discussion of an alternative, potentially safer method of farming.

Environmental Protection Agency

Rachel Carson's research on environmental contaminants contributed to a heightened public and political awareness of pesticide hazards (https://babel.hathitrust.org/cgi/pt/search?q1=Rachel%20Carson;id=mdp.39015022635984;view=1up;seq=11;start=1;sz=10;page=search;orient=0). Pollution control became a critical national issue, but it became glaringly obvious that federal environmental pollution regulation and oversight was inefficient and ineffective. Pollution control was fragmented between multiple departments and accountability gaps and overlaps in addressing environmental issues were common. In addition, most of the federal department's goals focused on other priorities, leaving environmental issues as a bi-product or secondary concern. The system, as it was, challenged the U.S. government's capacity to effectively research, regulate and mitigate environmental hazards. In response, President Nixon's Advisory Council on Executive Organization proposed a new Administration solely responsible for protecting the nation's environmental integrity and the public health from environmental hazards. To do this, the Council on Environmental Quality was merged into the newly formed EPA in 1970. In addition, an integrative set of environmental responsibilities was reallocated from the following administrations and programs were combined into one administrative body—the Environmental Protection Agency (EPA):

- Federal Water Quality Administration of the Department of Interior (DOI),
- Pesticides Research and Standard-Setting Programs of the Food and Drug Administration (FDA)

- Pesticide Registration Program of the Agricultural Research Service of the Department of Agriculture (USDA),
- Environmental Control Administration, National Air Pollution Control of Health, Education and Welfare (HEW), and
- Radiation Protection Standards (certain functions) of the Atomic Energy Commission (AEC). (https://www.epa.gov/aboutepa/ash-council-memo)

The goal of the EPA—to "establish and enforce environmental standards consistent with national environmental goals" — plays a significant role in protecting public health and the environment (https://www.epa.gov/aboutepa/ash-council-memo). But from the start, it was known that the EPA would be operating "on the horns of a dilemma" as an advocate and enforcer for public and environmental health in the face of the economic progress that matches, and perhaps also drives, our accustomed or desired standard of living. As stated in the Ash Council Memo for President Nixon which initially laid out the rationale and structure for the EPA, a

> [s]ound environmental administration must reconcile divergent interests and serve the total public constituency. It must appreciate and take fully into account competing social and economic claims…[in order to] sustain a well-articulated attack on the practices which debase the air we breathe, the water we drink and the land that grows our food. (https://www.epa.gov/aboutepa/ash-council-memo)

Food and Drug Administration

Regulating approximately 80% of the total gross national product, the Food and Drug Administration (FDA) is responsible for ensuring that commercial food is safe to

consume (except meat, poultry and eggs which are the USDA's responsibility). The FDA is mainly concerned with post-market safety, meaning that once a food is commercially available to the public, the FDA is responsible for carrying out regulatory standards that ensure it is safe for human consumption or protective measures if it is found to be toxic.

Introducing Agricultural Biotechnology

Genetically modified, GMO's, bioengineered, transgenic and genetically engineered (GE) are all different ways to talk about the same thing—the seeds/plants which have been modified through r-DNA techniques, which is, according to the U.S. National Institute of Health, "foods [that] have had foreign genes (genes from other plants or animals) inserted into their genetic codes" (www.nlm.nig.gov/medlineplus/ency/article/002432.htm). This is a key distinction from traditional plant hybridization which develops new varieties and traits by crossing genes from the same plant family.

Company Histories

Since the 1990's, the bio-agricultural industry, however, has experienced great economic gain. Between 1994 and 1997, the USDA granted non-regulated status for a variety of genetically engineered crops from a handful of industry manufacturers: Calgene (tomato, cotton and rapeseed); Upjohn (squash); Monsanto (soybean, potato, cotton; tomato; corn-glufosinate tolerant); Zeneca & Petoseed (tomato); Ciba Seeds (corn—insect resistant); AgroEvo (corn—glufosinate tolerant); Dekalb (corn-glufosinate tolerant); etc. There were approximately a dozen crops that the USDA had determined non-regulated status by the time Monsanto petitioned for non-regulated status for GA-21

(the glyphosate tolerant pre-cursor to NK603). In Monsanto's (and DeKalb Genetics Corporation) petition to the USDA, Mutz, et al. (July 30, 1997) emphasized GA21's "environmental and safety characteristics", describing glyphosate as not only highly effective for weed control during the growing season, but it binds to the soil thus reducing leeching (and runoff contamination), biodegrades quickly and has "extremely low toxicity to mammals, birds and fish" (p. 2).

But GA21 did not start with Monsanto. Bayer Crop Science, S.A. used to be Rhone-Poulenc Agro, S.A. (formerly or currently also Aventis Crop Science, SA, (http://bayercropscience.com.au/cs/ourcompany/). Rhone-Poulenc Agro (R-PA) and Dekalb collaborated, for years—R-PA did initial genetic work on the seeds and Dekalb inserted the genes and grew the plants. R-PA developed glyphosate resistant corn and patented the genetically modified trait (RD-125). However, in 1994, R-PA "gave" (this later gets decided in court that the rights were obtained fraudulently) Dekalb rights of use as well as rights to grant sublicenses and in 1996, Monsanto became a significant (40%) equity interest owner (with 10% voting stock) in Dekalb and soon obtained a sublicense to grow glyphosate resistant corn using R-PA's RD-125 technology. Part of the agreement between R-PA and Dekalb was that Dekalb would report the results of the field tests to R-PA. However, in 1994, Dekalb withheld the results (which confirmed greenhouse results of glyphosate resistance 4 times the goal expectations set by Monsanto) and instead wrote to R-PA asking permission to use RD-125 with soybeans (http://www.uspto.gov/web/offices/com/sol/ambriefs/Monsanto.pdf l).

Coincidentally, in 1996 Monsanto put their first glyphosate-tolerant crop on the market—Roundup Ready soybeans (http://www.monsanto.com/food-inc/pages/seeds-patent-history.aspx). Withholding the field test results (of the RD-125 corn) from R-PA, DeKalb began using plant breeding techniques to make the genetically modified glyphosate-tolerant corn a more durable and consistent line. Between 1994 and 1996 Dekalb had developed the first Roundup Ready corn line (GA21) using R-PA's RD-125 and Monsanto began selling it in 1998. Dekalb Genetics Corporation, since 1998, is a fully-owned subsidiary of Monsanto, and one of the leading corn seed suppliers in the U.S. (http://caselaw.findlaw.com/us-federal-circuit/1136223.html). That year (1998), Monsanto's Robert Fraley, Robert Horsch, Ernest Jaworski, and Stephen Rogers were awarded the National Medal for Technology and Innovation (NMTI) "[f]or their pioneering achievements in plant biology and agricultural biotechnology, and for global leadership in the development and commercialization of genetically modified crops to enhance agricultural productivity and sustainability" (http://www.uspto.gov/about/nmti/recipients/1998.jsp). This reward pairs well with Monsanto's John F. Franz' 1985 NMTI "[f]or his discovery of the herbicidal properties of glyphosates which have had significant consequences upon the production of agricultural food and fiber as well as upon agricultural practices throughout the world" (http://www.uspto.gov/about/nmti/recipients/1985.jsp).

NK603 and Roundup

The trade name for NK603 corn is "Roundup-Ready Corn" and has been sold alone as an herbicide (Roundup) tolerant seed or as a seed that is a combined (stacked)

with other GMO traits that offer herbicide tolerance and insect resistance. The patent for NK603 expired in 2015 and in response Monsanto has developed and is marketing a new version, Roundup Ready 2, which allows a broader timespan to spray and tolerates a higher rate of herbicide application (http://deltafarmpress.com/monsanto-new-roundup-ready-corn-2-system). There is some confusion, however, in defining Roundup Ready 2 in regards to earlier reference that distinguished NK603 as Roundup Ready 2 from its predecessor, GA-21 (the original Roundup Ready corn). For the purpose of this study, NK603 is Roundup Ready and the study includes an investigation into Roundup Ready 2 corn with the assumption that the knowledge creation, transformation and dissemination process for each is comparable because the product is marketed as a somewhat equal replacement for the patent-expired NK603. In other words, Roundup Ready 2 is virtually the same as NK603 but Monsanto was able to obtain a separate patent because it attached the glyphosate tolerant gene to a different "promotor" in the gene sequence (Lawson and Charnley, 2016). Both NK603 and Roundup are property of Monsanto and currently approved by over 20 countries around the world, including the U.S., Canada, European Union, China, Japan and the Russian Federation and they are promoted as safe for human consumption (assuming Roundup is not consumed directly but as a residue).

Roundup is a brand name for the pesticide that Monsanto developed as part of the herbicide tolerant corn system. Its main ingredient is glyphosate and the Roundup formulation is glyphosate mixed with "other" ingredients—adjuvants and surfactants. One of these surfactants is polyethoxylated tallowamine (POEA), of which several Roundup formulas contain. POEA's have become a central part of the conflict with rising

concern regarding its impact on human, aquatic and animal health. But without surfactants, such as POEA's, glyphosate would not be as effective as an herbicide. What makes the glyphosate plus surfactants/adjuvants so effective (I will use POEA's here as an example since it is part of the conflict) is that when glyphosate is applied to a plant, the salt and POEA enhance the chemical's ability to drive into the cells of the plant , enabling the chemical to travel through the leaves, down the stem and to the roots and shoots and from there it can enter into the soil, biodegrading into its major metabolite, (i.e. the major component left after glyphosate breaks down)—aminomethylphosphonic acid (AMPA). Glyphosate binds very well to certain types of soil (less sandy), biodegrading (according to some) within a few weeks and, therefore, is marketed for being a low-risk pesticide for run-off contamination. The two products, Roundup and NK603 (and its stacked versions) are widely marketed as a safer, more environmentally sound alternative for weed control than other, more hazardous conventional solutions.

Séralini

This dissertation focuses on the agricultural biotechnology research and policies surrounding a recent study conducted by Gilles-Eric Séralini, et al (2012) (representing researchers independent of the bio-agriculture industry) and the subsequent conflict arising from industry-related scientists, government bodies and Monsanto regarding Séralini's, et al (2012) work. Séralini's, et al (2012) study examined the long-term toxicity of a specific variety of NK603 and the herbicide Roundup with which the corn is designed to work. Using Séralini's et al (2012) study will provide a basis of understanding the broader issue of food safety testing, assessment, policy and regulation.

Séralini and his team argued that approval for these products was based on the Organization for Economic Cooperation and Development's (OECD) internationally accepted 90-day standard for sub-chronic toxicity tests and does not, subsequently, demonstrate long-term safety. To compensate for this gap in the research, he and his team designed a 2-year chronic toxicity test that expanded on a previous industry-led (Monsanto's) 13-week study on NK603 from which Séralini had interpreted changes between the control and test animals indicating potential toxicity. Séralini et al (2012) emphasized that theirs was the only study, to date, that examined long-term toxicity of NK603. In addition, Séralini et al (2012) noted that, prior to their research, studies on herbicides typically examined the main ingredient in Roundup, glyphosate, but not the product as a whole which would include the adjuvants that enhance the capacity for glyphosate to work. They submitted the results of their study, titled "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize" along with photos of rats with large tumors, concluding that the results of their study indicated that NK603, Roundup and glyphosate were toxic and that additional long-term studies were necessary to confirm or reject their initial findings.

Shortly after Séralini's study was published in Food and Chemical Toxicology journal, letters of protest to Séralini's article began to populate the journal's editorial section, emphasizing "concerns about the validity of the findings it described; the proper use of animals; and even allegations of fraud" (http://www.elsevier.com/about/press-releases/research-and-journals/elsevier-announces-article-retraction-from-journal-food-and-chemical-toxicology). Séralini was asked by the journal's Editor-in-Chief, A.

Wallace Hayes, to submit all of his team's research data for review and Hayes commended him on "his willingness and openness in participating in this dialog"; however, after a thorough review, the journal's Editor-in-Chief "found no evidence of fraud or intentional misrepresentation of the data…but, ultimately, the results presented (while not incorrect) are inconclusive, and therefore do not reach the threshold of publication for Food and Chemical Toxicology" (ibid). The European Food Safety Authority also reviewed Séralini's, et al (2012) study and concluded that the study design and the presentation of the data negated any conclusions of carcinogenicity (EFSA, 2012). Prior to the article retraction, Richard Goodman, who was identified by several anti-GMO groups (gmoanswers.com; march-against-monsanto.com; gmwatch.org, etc.) and confirmed by the Editor-in-Chief, as a former Monsanto employee, was hired as part of the editorial board (https://www.elsevier.com/about/press-releases/research-and-journals/food-and-chemical-toxicology-editor-in-chief,-a.-wallace-hayes,-publishes-response-to-letters-to-the-editors). In a written response to a multitude of complaints about industry pressuring the journal to retract the article, Hayes announced that the journal's editorial board consisted of "academic, government, and industrial scientists", emphasizing that Hayes was hired for his scientific expertise and that his appointment as Associate Editor, as well as the article retraction, "was not influenced by Monsanto, or any other party" and the decision to retract Séralini's article was his (Hayes') alone (ibid, p. 1). In addition to perceptions of conflict of interest, Hayes's response addressed complaints that questioned why an article describing a 90-day study that Monsanto had previously submitted was not also retracted, (this was the study that Séralini, et al were

replicating). He distinguished Séralini's study from Monsanto's study mainly in terms of the language used to describe the purpose and what each study claimed as their outcomes. Hayes stated that Séralini's claim that their study potentially linked NK603 and Roundup to cancer was unsupported by the data as well as the design of the test, whereas Monsanto's claim of safety was supported by the design and the data (ibid). Séralini had responded to this claim, noting that in the article, it is explicit that the study was chronic, not carcinogenic, and therefore met the design criteria, but did not preclude them from presenting evidence of potential carcinogenicity and suggesting further studies to determine the validity of those initial findings. Comparing Séralini's research article to the journal's "Guide for Authors", "Publishing Ethics", and "Article Withdrawal" policies, the article technically meets the journal ethical standards and publication requirements (https://www.elsevier.com/journals/food-and-chemical-toxicology/0278-6915/guide-for-authors#8101; https://www.elsevier.com/editors/publishing-ethics; https://www.elsevier.com/about/company-information/policies/article-withdrawal). To access the letters to the editor and subsequent response pieces, see http://www.sciencedirect.com/science/article/pii/S0278691512005637.

The heart of the issue appears not to be whether or not Séralini's study is inconclusive, but rather how science is conducted, interpreted and used. With this as a foundation, the resulting knowledge becomes a potentially powerful tool for industry, government and public policy development. Following the retraction of Séralini's study, the bio-agriculture industry representatives and U.S. government representatives have defended the integrity of the safety tests that support current public policy regarding

NK603 and Roundup, but the European Food Safety Authority (although not accepting the validity of Séralini's study) and the European Commission have indicated the potential need for long-term feeding studies and, more recently, a re-evaluation of Roundup's main ingredient--glyphosate.

My initial investigation into this case reveals contexts within contexts that integrate science with political, environmental, economic and social issues. However, to limit and focus the scope, this study will mainly focus on political, economic and social issues. For example, it seems that, according to Domingo and Bordonaba (2011), Diels, et al (2011), and Fernandex-Cornejo (June 3, 2010), most legislative and regulatory decisions surrounding Monsanto's NK603 corn and Roundup are made based on industry-backed research. Séralini's case potentially challenges the safety of two of Monsanto's key products, thus challenging the integrity of the science currently backing the safety of those products and the status quo of public policy regarding those products, which ultimately impacts society at the consumer level.

Statement of the Problem

The integration of multiple forms of genetically modified food into the global food system assumes a level of safety for human and animal consumption. Government policies and regulations regarding how these food products can be disseminated in the global market rely mainly on industry-based research (and interpretations) of their results. However, there are other scientists who argue that their own research suggests that certain genetically modified foods (and the pesticide/herbicide applications with which they are designed to work) are potentially unsafe for human and animal consumption.

Both sides claim the other's research is inherently biased, insufficiently designed and tested, and inconclusive and/or invalid. The disagreement between researchers regarding the science (e.g. research design, methodology and interpretation of outcome) of genetically modified foods safety testing, impacts local to international government and civil society responses to whether and how genetically modified food should be tested and regulated.

Purpose of the Research

Reasons for conducting this study are threefold: 1) corn is a major crop that impacts U.S. and global economies, health and environment, 2) NK603 corn (whether it is grown as a single GE trait or stacked) makes up a significant percentage of corn crop acreage and Roundup is one of the most widely used agricultural herbicides, and 3) the on-going controversy between scientists, government and industry regarding the safety of these products suggests there is a potential red flag in the scientific-industry-government triangle of knowledge production, dissemination and implementation.

The purpose of this research is to present the data and analysis within a systems-oriented socio-political perspective. I am trained as a social scientist, not a lab scientist; therefore, I examined the scientific elements inherent in the topic (e.g. research design protocols and the basic research design features of Séralini's case) as a layperson. My purpose for conducting this research was not to validate or discredit scientific research, but rather identify social and/or political processes that impact scientific research and vice versa. I examined systemic processes between researchers, private interests and government policy makers in the development of research protocols, policies and

regulations for Monsanto's NK603 corn and Roundup and related agricultural biotechnology. Although the main focus of the research is U.S. government policy, Yin (2004) reminds us that national policy is often set in international context. Thus, this research also examined case-related international policy processes, particularly those within the Organization of Economic Cooperation and Development (OECD), the World Trade Organization, the European Commission and European Food Safety Authority. Not only is the European Union (EU) the setting in which Séralini's research takes place, but EU (a significant importer of genetically modified corn) internal policies regarding bio-agricultural technology often clash with U.S. international commerce expectations.

Propositions

1. My first proposition is that there are certain critical factors that contribute to the conflict. On the surface, these factors include:
    - potentially inconsistent research protocols,
    - limited public access to raw data and flexible interpretations of subsequent statistics,
    - perceived divergence/alignment between research results and public policy/regulatory decisions,
    - transparency in how public policy and regulatory decisions are made, and
    - rigid positions from outlying anti- and pro-bio agriculture groups. Underlying these factors are issues of trust, values, interests, ethics, rights and power. From a conflict analysis perspective, this

case is significant because it examines current assumptions about the credibility and validity of Science as it pertains to public policy-making, public health and private interests.

2. My second proposition is that there are potential patterns of knowledge transformation from the research stage to policy regulation. This is important as a potential learning tool for current and future conflicts that involve public safety and private and/or government interests. Finding patterns enables us to better compare this particular topic to the larger scope of food safety as well as the broader consequences and benefits of other policy issues involving public safety (Yin, 2004)
3. My third proposition is Séralini's study, through its contribution that challenges the politically determined standardization of agricultural biotechnology toxicology testing, represents a pivotal shift in how agricultural biotechnology is researched and perceived as valid by illuminating the "crisis" in critical, yet potentially unresolved, problems.

Research Questions

How do science and industry influence state-level policy and regulatory decision-making processes regarding the safety and/or promotion of a specific genetically modified corn (NK603) and the herbicide (Roundup) with which it is designed to work? How and what knowledge is generated and how is it transformed between scientists, industry and government to create policies and regulations for production and consumption of NK603 corn? What are the possible benefits/consequences of current safety protocols and how

are those protocols met or challenged by Séralini's research team's study? How does Séralini's study compare with other major public policy processes, specifically compared with DDT and lead?

Theory and Ethics

Underlying the language of policy, industry, and science is a common social denominator. Stake (1995) suggests that "[t]o the qualitative scholar, the understanding of human experience is a matter of chronologies more than of causes and effects" (p. 39). This seems to make sense if one considers the complex interconnected systems that help create social events. Within the context of scientific research, public/private interests and needs, and public policy, cause and effect is not easily determined because of multiple direct and indirect influential factors that impact outcomes within that chronology—so a comprehensive chronology is more multi-dimensional than linear. But with the realization of such complexity, how can chronology offer any more explanation or understanding if we do not create a subjective perspective from which to construct and understand those events? Mayring (2000, p. 12) offers a bridge between ideologies of objectivity and subjectivity by suggesting that we bracket our prior understandings, attitudes and assumptions by "stay[ing] persistently curious about new phenomena". Without bracketing one's own bias, there is increased potential that the research gathered to create the foundation of analysis is also biased, and therefore less credible. In other words, I strived to limit my bias by consciously opening my mind to new possibilities and new perspectives. I willingly sought to broaden the boundaries of my personal realities in order to achieve a more holistic understanding of the phenomenon.

Social construction.

This study is important to help understand how information is shaped and used from its creation within the research lab to its implementation in public policy. Why this information is so important is because in the U.S. and other major Western societies, science and scientific process is highly valued as a determinant of truth and fact. It helps these cultures determine the boundaries of reality. Integral to creating these boundaries are how our ideologies help shape our worldviews and what we value; when one group's ideologies conflict with another group's ideologies, there is, as Gergen (2009) suggests, a tension between insiders and outsiders, us v them, right v wrong which lends to a negative perception of the "other". How one constructs perceptions of scientific validity could be perceived as stemming from socially constructed transitions from, for example, religious and political autocracy to Enlightenment and the "rise of science, objectivity and truth" (Gergen, 2009, p. 27). However, Gergen (2009) also emphasizes that science, objectivity and truth have not only the capacity to empower, but also to dominate as we construct "knowledge class" of haves and have nots in which access to the knowledge creation (and the knowledge itself) is restricted to privileged individuals and/or groups (ibid). The exchange of knowledge within and between scientists, industry, policy makers and the public occurs within a social context.

Using social construction as one of my theoretical foundations in thinking about the conflict within this case, the tension between scientists, industry and government is maintained by conflicting ideologies, values, and interests that have been constructed through social (e.g. human) interactions. Alternatively, when differing socially

constructed realities meet, there is an opportunity to invite change and to allow one's worldview, ideologies, values and interests…one's boundaries of reality…to shift. Throughout this research there is a consistent thread of relationships and social interactions that influence how science is conducted, how it is assessed and how it is delivered and received in a broader social context.

Scientific revolution.

Researching from a social construction perspective is complemented by considering Kuhn's (1996) theory on scientific revolution. "[D]uring revolutions, scientists see new and different things when looking with familiar instruments in places they have looked before" (Kuhn, 1996, p. 111). According to Kuhn, the science that society accepts as "normal" is simply the current trend in how to conduct and interpret valid scientific research. Sowell (2007) describes these trends as "visions" that mold and establish our moral, political, economic, religious and social ideas. That is, until an anomaly challenges the current trend's capacity to solve a significant problem, which leads to a scientific "crisis" in which new methodologies and theories are tested until something succeeds at solving a piece of the puzzle. This, in turn, leads to a "paradigm shift" in which the previously validated theory and methodology is replaced with something unexpected that requires a new theory and method to be developed to explain/solve that piece of the puzzle (http://bertie.ccsu.edu/naturesci/PhilSci/Kuhn.html; https://www.uky.edu/~eushe2/Pajares/Kuhn.html). What might cause this revolution is a juncture between conflicting paradigms that challenges current standards. But if there is discrepancy between what some policy makers, scientists and public consider valid in

terms of current standards as in the case of agricultural biotechnology, the transition remains in "crisis" until a solution is found that resolves the "problem" and is accepted and mainstreamed by the general population. Sowell (2007) suggests that visions form the basis upon which the theories and hypothesis surrounding perceived problems and solutions are framed. When a scientific "crisis" occurs, Sowell (ibid) suggests that, in theory, divergent conclusions can be checked and verified by scientific processes. However, Sowell, in suggesting why this verification process might be hindered, states that "[a] great deal of partial evidence may be accumulated on each side, but the evidence for and against one's own vision can be weighed differently, and being convinced is ultimately a subjective process" (p. 232).

Séralini and his team were not the first researchers to question scientific anomalies resulting from past toxicology studies and they were not the first to conduct toxicity studies that challenge the status quo of genetically engineered crop and pesticide safety, so how might Séralini's case be different? Séralini and his team challenged the status quo of a significant research design protocol (90-day toxicity studies) not only by explicitly questioning the validity of current scientific standards but by producing a study that potentially challenges the status quo of current public policies and industry ideologies. According to Sowell (2007), a party responding negatively to evidence (e.g. through "denial, evasion, and obfuscation") indicates a level of threat that the evidence represents. In the case of Séralini, it might be perceived that divergent visions of "sound science" are being challenged by the evidence presented in Monsanto's study versus the evidence presented in Séralini's study (p. 233). Sowell (ibid) goes on to state that "[a]t

one extreme in the relationship of evidence to visions is the total subordination of evidence to conclusions based on a vision or the theories deriving from it" (p. 233). Operating outside the social constructs of industry and government offered Séralini and his team a different perspective from which to accept and or question the science and policies of NK603 and Roundup, and their study, with the help of mainstream media, offered a sort of spotlight that highlighted the larger conflict in which other independent scientists could join regarding how, what, and why certain scientific assumptions are considered valid, or not. It is possible, however, that this case ends with circular arguments from conflicting parties about, as Kuhn (1996) puts it, "what is a problem and what [is] a solution" (p. 109). But, I feel optimistic that these conflicting systems and worldviews are somehow converging and that change is inevitable.

Critical theory.

Anticipating this change, critical theory is influential to my perspective and played a significant role in how I analyzed the system dynamics within the context of knowledge, power and social change within and between two major democratic bodies (U.S. and E.U.). I analyzed how power is defined and used to create and transform knowledge for agricultural biotechnology science and policy. Applying critical theory to this study suggests that the system, to some extent, currently supports social oppression (or knowledge repression) and that "[o]ur knowledge of material "facts," for example, cannot be disconnected from the social understandings or interpretations of those facts…" (Payne and Samhat, 2004, p. 14). Using a more Habermasian interpretation of critical theory, in which not just mainstream media, but also interpersonal communication

develops public thought and understanding, I sought to identify where, in these system dynamics, are potential points for knowledge transparency and, therefore, social change that integrates a more balanced approach to economic, political and social health (http://people.ucalgary.ca/~rseiler/critical.htm). An integral part of shaping public policy in a democracy is creating opportunities of developing shared understanding and or illuminating knowledge discrepancies within and between public participants. Habermas' critical theory suggests specific criteria that need to be met for public communication and understanding to occur:

- adequate opportunity for people to speak,
- adequate opportunity to challenge the rules or the topic of discussion,
- adequate opportunity to acquire the skills of discourse (including those of the media), and
- adequate opportunity to be free of violence and other forms of coercion. (http://people.ucalgary.ca/~rseiler/critical.htm)

My research illustrates how these criteria are currently met and not met in developing the science and public policy for agricultural biotechnology. I chose this study because of the controversy surrounding the design and outcome of Séralini's research and how this controversy links concepts of credible and valid science to the creation and use of knowledge in case related policy and regulation for consumer and industry protection. Critical theorists recognized the challenge in public enlightenment when technical rationality (in this study I will focus on the government and industry use of "sound science") "on the one hand…was a critical arbiter and espoused the ideal of

impartial analysis of truth and on the other hand it became the instrument of perpetrating domination of nature and humans by technicalising administrative, political, and bureaucratic processes" (http://www.unipune.ac.in/snc/cssh/ipq/english/IPQ/21-25%20volumes/25%2002/PDF/25-2-7.pdf). Overall, critical theory, as it is used in this research, seeks to explain social ideologies in terms of "human emancipation through consciousness and self-reflection" by "evaluating the rationality of any system of domination in view of certain standards of justice" (http://www.iep.utm.edu/frankfur/). In this study I will analyze the role agricultural biotechnology plays in whether/how individual, institutional, state and corporate security (as it pertains to independence, power and status) impact the transformation of knowledge.

Systems theory.

In order to analyze such complexity, I have conducted my research through the lens of systems theory, framing my analysis of how science, industry and politics influence, and are influenced by, each other in terms of interrelated elements of a complex web—identifying and analyzing the dynamics between access points of influence, outcomes generated, feedback loops, delays and leverage points (Meadows, 2008). Systems theory in regards to science and public policy development could be interpreted as a challenge to scientific validity if one perceives science as the means to "explain observable phenomena by reducing them to an interplay of elementary units investigable independently of each other" (http://www.panarchy.org/vonbertalanffy/systems.1968.html). Agricultural biotechnology as is it regulated in the U.S. could be argued to support such a classical

worldview as plant DNA parts, although considered complex, are replaceable because the plant system is assumed to be mechanistic and the mechanisms are assumed (by some) to be understood and predictable in identifying a piece of the puzzle. But it does not describe the whole picture. Systems theory seeks to integrate "elementary units" within a broader dynamic context in which the parts are analyzed in relation to the whole (Meadows, 2008; Laszlo, 1996; http://www.panarchy.org/vonbertalanffy/systems.1968.html). Systems theory is integral in my research and analysis because it provides an opportunity to discover how the parts: the research, the relationships, the perceptions and the public policy interact and influence each other to maintain and/or change the system within which they operate. It also provides a foundational assumption that public policy that utilizes scientific data as a basis for decision-making potentially inhibits the system within which it operates, if the "elementary units" of scientific data are insufficient to effectively exist within the broader social and environmental contexts.

Taking into consideration that a researcher's selection of data is not a complete picture, the best I can offer is a perspective (a version—a socially constructed reality of how things happen or what "actually" happened). Thus, it becomes necessary to triangulate a variety of perspectives, integrating and respecting the voices and values of relevant stakeholders in order to create a more balanced representation of "reality". Throughout this process, it is also my responsibility and priority, as a researcher, to maintain consciousness of, and strive to minimize (if not eliminate), personal biases throughout the research process.

Chapter 2: Literature Review

Background

Introduction

Genetically modified, GMO's, bioengineered, transgenic and genetically engineered (GE) are all different ways to talk about the same thing—the seeds/plants which have been modified through r-DNA techniques, which is, according to the U.S. National Institute of Health, "foods [that] have had foreign genes (genes from other plants or animals) inserted into their genetic codes" (www.nlm.nig.gov/medlineplus/ency/article/002432.htm). Within this text, agricultural biotechnology refers to the agricultural system that utilizes genetically engineered crops and the chemical applications with which they are designed to work. This system is often referred to within the context of innovation and technology. Agricultural bio-technology industry refers to the companies that develop and market genetically engineered seeds (and the chemical pesticide applications with which they are designed to work). To clarify the distinction between hybridization and genetically engineered food, the process of inserting foreign genes distinguishes genetically modified food from food that has been modified through hybridization (which manipulates genetic qualities through same-species modifications). The development and promotion of food innovation technologies is currently being promoted as a viable solution to the overuse of chemical agricultural applications as well as a potential solution to food shortages across the globe.

Since corn is a significant commodity for the U.S. economy, the policies and regulations surrounding its evolution from seed to consumer have a major impact on the

industries that research and develop seed varieties as well as the farmers who grow them, the environment they're grown in, and the consumers (human and animal) who eat any of the corn products available on the market. Balancing risk with benefits is not simply about consumer and environmental health, but also about the economic health of the agricultural industry and national interests that extend from local to global contexts. The economic, environmental and social implications of biotech corn production, trade and consumption make it a key target for public, private and political debate. Innovative food technology seems to be a key factor in maintaining U.S. economic and political status as a global leader.

According to Kogan (2007) and the USDA, biotechnology in agriculture has gained prominence within commercial and industrial markets and promises a level of political power in terms of increasing economic advantage within the international market (http://www.usda.gov/documents/BIOTECHNOLOGY.pdf, n.d.). However, Domingo and Bordanaba (2011) note in their study that much of the published research promoting GM varieties as safe was conducted by "biotechnology companies or associates, which are also responsible [for] commercializing these GM plants" (p. 741). According to the USDA, the science involved in testing the safety of specific bio-agricultural products is not free from external influence, but rather it is part of a system in which the needs and interests of industry, national governments and the public compete (USDA Office of Communications, March 2003).

Crop Significance

According to the most recent Prospective Planting survey, corn is arguably the most significant commercial crop grown in the U.S. with total crop acreage equaling 93.6 million acres (USDA NASS, March 31, 2016). This is impressive, considering that from 1900 to 1956, corn crop acreage decreased by approximately 40 million acres (94.9 million acres to 54.6 million acres) and has gradually regained that acreage throughout the last sixty years with about 25% of that gain in just the last five years (According to the National Corn Growers Association, approximately 31% of total U.S. harvested crop land is used to grow corn (http://www.nass.usda.gov/Charts_and_Maps/Field_Crops/index.asp). According to Fausti (2015), the Federal Agriculture Improvement and Reform Act of 1996, aka The Freedom to Farm Act, offered payment incentives that made farming at a large scale more affordable, and a series of biofuel policies offered "motivation [that] opened the door for producers to adopt a corn/soybean monoculture production system" (p.2). According to Weeks (1992), however, "[w]hen a city or nation has only one or two major industries or exports, it is quite vulnerable to economic downfall when that one industry or export suffers hard times" (p. 35). Currently, there is more corn produced in the U.S. than all the other grain crops combined and it is, by far, the largest feed crop in the U.S. more commonly grown for human consumption and industrial uses (Capehart, Oct. 16, 2014). It is processed into starch, oil, alcohol, sweeteners and ethanol fuel (ibid). As the global leader in corn production, the U.S. is also the leading trade partner in international corn and coarse grains trade, with 20% of U.S. corn crops being exported (which

accounts for a total of 32% of the world's corn) (Capehart, Oct. 16, 2014; http://www.epa.gov/agriculture/ag101/cropmajor.html, Apr. 11, 2013).

Herbicide Tolerant Corn

Of the approximate 90 million acres of commercial corn that is grown in the U.S., 92% is genetically modified to be herbicide tolerant (Fernandez-Cornejo and Weschler, July 9, 2015). Of the eleven most commonly used herbicides in U.S. commercial agriculture (plus one category generalized as "other"), glyphosate accounted for 38% (Fernandez-Cornejo, Osteen, Nehring, and Wechsler, June 2014). Since its introduction into commercial agriculture, glyphosate (the active ingredient in Roundup) has dominated the market for herbicide applications, mainly because of the widespread adoption of genetically engineered herbicide tolerant crops (i.e. Roundup-Ready crops) that are designed to tolerate glyphosate. However, single-trait Roundup-Ready crops are not the only GMO crops designed to withstand glyphosate applications; the market for genetically engineered seeds has broadened from single trait seeds (e.g. seeds engineered to internally produce a specific insecticide *or* seeds that are tolerant of a specific herbicide) to seeds with stacked traits, making them resistant to, for example, to a specific type of insect or fungus *and* tolerant of herbicidal (specifically glyphosate) applications. This means that Monsanto, in addition to other major agricultural bio-technology companies, such as Dow and Syngenta, among others, are producing a variety of crop options that can withstand glyphosate applications. The patent expiration of Roundup Ready corn (mentioned above) opens market opportunities for generic brands

of Roundup tolerant corn, potentially increasing the amount of glyphosate tolerant corn that is already grown as farmers will be able to save generic seeds for replanting.

But Roundup is not limited to genetically engineered crops; Roundup, and other glyphosate formulations, can also be applied, in diluted concentrations, to conventional crops (as well as in forestry applications, ditches and golf courses, lawns, etc.) as a "plant growth regulator". In fact, prior to the introduction of the first Roundup Ready crop, the 1993 EPA Reregistration Eligibility record lists numerous types of crops (twenty-nine) on which glyphosate was applied (EPA, Sept. 1993). When used in this capacity, glyphosate formulations are usually applied just prior to harvest as a means to modify plant growth and expedite the ripening process (http://www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/red_PC-417300_1-Sep-93.pdf).

Genetically modified herbicide corn became an attractive alternative to conventionally grown corn for farmers looking, in part, to reduce the amount of herbicide application necessary to effectively combat weeds and, in turn, increase their crop productivity and improve environmental quality of local land and water resources. With widespread adoption of Roundup Ready crops and subsequent use of Roundup and other glyphosate products, several weed varieties have grown tolerant as well to glyphosate. With Monsanto's Roundup Ready 2 corn line, farmers will be able to address this problem by applying higher rates (within EPA standards) and extending the number of times they apply herbicide. The USDA's Economic Research Service found that in 1996 (when herbicide tolerant crops were first introduced), herbicide applications on U.S. corn

crops initially decreased but then increased in subsequent years (Fernandez-Cornejo, Wechsler and Livingston, March 04, 2014). Between 2002 and 2005, glyphosate application rates increased five-fold while corn crop acreage only increased three-fold for the same time frame (http://www.centerforfoodsafety.org/files/2009-glyphosate-registration-review--final-9-21-09_48080.pdf).

Science and Public Policy

From a historical perspective, there is cause for public concern when a new agricultural technology enters the market that could potentially harm public health. For example, the lag time between the first reports of negative health effects and effective government legislation and regulation of products, such as with DDT and lead, can be decades to over a century apart, respectively (Kraft and Kamieniecki, 2007; Murray, 1983). In the meantime, according to Domingo and Bordanaba's research reviewing GMO safety testing, for about the first decade of testing, the majority of research on genetically modified food safety weighed in favor that GMO's were safe, but in recent decades, there appears to be an increasing balance between research groups that promote genetically modified products and/or their chemical counterparts as safe and research groups that indicate that there is a serious cause for concern (Feb. 5, 2011).

Considering that as of Sept. 29th, 2000, the USDA determined a "non-regulated status" for NK603, it seems critical to analyze how policies change when/if new scientific information challenges the validity of those policies (http://www.aphis.usda.gov/biotechnology/petitions_table_pending.shtml). However, Sowell (2007) offers a precautionary note suggesting that "evidence need not be falsified

in order to be evaded" (p. 233). Sowell (ibid) goes on to suggest that visions (e.g. economic progress, political strength, concepts of innovation, etc.) can be effectively protected from evidence to the contrary by being situated within the context of a theory that "may be so stated that nothing could possibly happen that would prove it wrong. In this case, the theory is reduced to the empirical meaninglessness; since all possible outcomes are consistent with it, it predicts nothing" (p. 233).

Snell's, et al (2011) study of the available research surrounding long-term (longer than 90 days up to two years) toxicity studies, also cross referenced available 90-day studies to see if there were significant differences in toxicology results in the long-term studies as compared with the 90-day studies. The authors concluded that while they noted small differences in some of the test results, there were no statistically significant changes in the long-term studies and, therefore, also concluded that 90-day studies were sufficient and that genetically modified food did not pose a risk to human health. But what is appropriate regarding the necessity perceived that would validate a long-term toxicity study is also under debate and is a key factor in whether Séralini's study is considered valid or unnecessary. A major factor contributing to the debate about genetically engineered crops is whether the internationally accepted norm of 90-day feeding trials is adequate to assume long-term safety. Proponents of current safety standards vouch for the 90-day feeding trial as sufficient time to demonstrate whether a product is safe or not (Agricultural Research Service, USDA, Feb. 23, 2015; Snell, et.al, 2011). But others, like Séralini, emphasize the need for longer studies.

Domingo and Bordanaba (Feb. 5, 2005) analyzed safety assessment studies of genetically modified plants from 2006-2010, as a follow-up to their previous study of published safety tests from 2000-2006. The purpose of their study was to qualitatively analyze current published studies regarding genetically modified crops that are grown for human consumption. They conclude that although the number of studies have grown considerably since their initial study (from 2000-2006), there is a relative dearth of comparable research, meaning that although there are a multitude of studies, there is a lack of consistency within the study design (e.g. length of study, specific parameters measured, type of study—rodent, avian, amphibian, dog, in vitro, etc.) which seems to me to be a potential factor driving conflicting perspectives. European Food Safety Authority joined U.S. political response to Séralini's et al (2012) research emphasizing methodological flaws in his research, stating that the "authors' conclusions cannot be regarded as scientifically sound because of inadequacies in the design, reporting and analysis of the study as outlined in the paper" as the reason for rejecting his claims and that the "EFSA finds there is no need to re-examine its previous safety evaluations of NK603 or to consider these findings in the ongoing assessment of glyphosate" (http://www.efsa.europa.eu/en/press/news/121128 ; http://www.efsa.europa.eu/en/press/news/121004.htm; http://gain.fas.usda.gov/Recent%20GAIN%20Publications/Review%20Of%20Seralini%20Paper%20By%20German%20Govt._Berlin_Germany_10-2-2012.pdf). Séralini, et al (2012), responded to critics of their study with an article that explained the motive behind conducting the 2-year study, the design methodology and detailed how it adhered to

OECD guideline 452 for chronic toxicity testing, and went further into detail regarding how their results, although not conclusive, suggested a need for further testing (http://www.gmoseralini.org/wp-content/uploads/2013/01/Seralinial-AnswersCritics-FCT_2013.pdf). However, Domingo and Bordanaba's (Feb. 5, 2005) reach similar conclusions as Heinemann (Nov. 6, 2012), finding that upon analysis, other GMO and/or glyphosate studies have been accepted as valid by scholarly reviewers and government representatives even though these studies indicate similar flaws, in research methodology, as was found in Séralini's et al (2012) research. Meyer and Hilbeck's (2013) comparative evaluation, of Séralini's study with two other (13-week and 90-day) NK603 studies, analyzes comparable design and reporting flaws that the EFSA considered sufficient to determine Séralini's study defective, but the authors point out that the other two studies (published by Hammond, 2000 and Monsanto, 2001) were not criticized for the same flaws. The authors suggest that this type of evaluative double standard needs to be addressed. Interestingly, the EFSA (June 3, 2015) recently posted a report detailing how they (the EFSA) will be improving their methods for evaluating science through increased rigor and enhanced consistency (http://www.efsa.europa.eu/en/press/news/150603.htm).

Since U.S. public food policy relies on science-based risk assessment, it seems critical that the assessment data and criteria for establishing scientific knowledge are derived from a balance of sources that meet the needs and interests of major public and private stakeholders. Such balance come into question if we consider the USDA's statements: "Agricultural biotechnology is rewriting the rules in several key areas—

agricultural policy, industry structure, production and marketing, consumer preference, and world food demand—and public policy is struggling to keep up" and "[c]ritical to the efficient and equitable advance of agricultural biotechnology is determining the unique role of public research and when and how the public sector should interact with the private sector" (USDA, Office of Communications, March 2003, p.8). Meyer and Hilbeck's (2013) research highlighted key points of divergence in how scientific knowledge is perceived by powerful government decision-makers. Their study was a comparative analysis of Séralini's el al (2012) study with two other NK603 studies—one a 13-week study and the other, including Monsanto's 90-day rat study that Séralini's team was replicating (but with a 2-year rather than 90-day duration). Meyer and Hilbeck (2013) also reviewed 21 other chronic toxicity rat studies. The result of their review concluded that there are "critical double standards in the evaluation of feeding studies submitted as proof of safety for regulatory approval to EFSA" as each of the three studies were comparable in their adherence or lack of adherence to the EFSA's testing criteria (p. 9). Although the scope of Meyer and Hilbeck's (2013) work is limited to the EFSA, their findings suggest potential factors that influence not only the EFSA, but also the decision-making processes of other policy-making bodies. The scope of both Snell, et al (2012) and Domingo and Bordanaba's (2011) research, each of which examined a multitude of safety assessment studies on genetically modified plants, are considerably broader than my topic and their studies did not incorporate Séralini's NK603/Roundup toxicity study. In addition, although each of their studies offered a comprehensive analysis of those safety assessments, their focus did not include a systemic analysis of how those studies

interconnect with research protocols, industry and public policy, indicating a gap in the research. Nevertheless, the results of their research illustrate the need for continued in-depth analysis of how science is interpreted and used to satisfy political, commercial and public needs and interests.

Science and Industry

But conducting scientific research and obtaining knowledge about bioengineered products is sometimes hindered by external factors such as patent rights, corporate protective measures (e.g. rules to protect privacy, property rights and confidentiality) and even narrowly defined federal research goals. Monsanto has maintained strict control over how its products are tested as a means to protect its investment. Controversy arises when the public's demand for unbiased (i.e. independent) studies conflicts with the industry's desire to protect its property and intellectual rights (Snell, C., et al, 2012). However, Monsanto suggests that securing patents for their products supports their (and other biotech companies) capacity for further innovation and, in turn, producing better products for farmers (http://www.monsanto.com/newsviews/pages/roundup-ready-patent-expiration.aspx).

What It Means for the Field of Conflict Analysis and Resolution

Developing national and international corporate networks and investments, according to Diamond and McDonald (1996), inevitably encourages companies to consider the "cultural, economic and political conditions" of its target market, but inevitably "[t]o improve its business success, it will naturally want to do what it can to protect its investment" (p. 54). According to Weeks (1992), conflicts often stem from

differences in what one considers as needs, values, interests and goals simply because the differences derive from an alternative perspective. Diamond and McDonald (1996) go on to describe that the basis for an increasing number of international "disputes, alliances, and posturing between nations" stem from geo-economies (i.e. "the integration of international politics and international business and trade") (p. 56). Weeks (1992) suggests that when parties perceive that their needs are incompatible with the needs of other parties, it increases the potential for serious conflicts. These conflicts may arise, for example, as parties ignore the needs of others or, in an effort to gain competitive advantage over others in order to meet their own needs, a party's actions hinder another's capacity to effectively meet their needs— "even when the needs are not as opposite or incompatible as they appear" (Weeks, 1992, p. 36). According to Diamond and McDonald (1996), businesses that are deeply invested in international trade and heavily influenced by certain trade policies "become, to some extent, both a party to emerging geo-economic disputes and a resource for their resolutions" (p. 56). Power (e.g. economic strength and political influence) is often a key factor in negotiating international diplomacy and, according to Diamond and McDonald (ibid), nations that perceive themselves to be in a position of strength will use "coercion, leverage, [and] threat" as a means to exert influence on another nation, and, within this system, "the nation itself, or its government, …is the vehicle of power" (p. 26). In other words, "we have developed an international system of relationships based primarily on the nation-state… [in which] [p]eoples, cultures, religious, ethnic or political identity groups and private citizens have no formal standing" (ibid, p. 26).

Policy changes that impact geo-political affairs, as suggested by Diamond and McDonald (1996), increasingly and systematically have been separated from public influence, lending to "the mystification of Track One [government level diplomacy] as a realm of unreachable experts" (p. 26). Although, according to the authors, there is "much relevant expertise about international relations, peace, and conflict resolution, the boundaries [that shield public policy makers from the general public] are so tight and so closely guarded that such expertise frequently has no way of getting through to the people who need access to it" (p. 30). Diamond and McDonald (1996) suggest that such barriers disrupt and/or hinder not only government to government attempts to analyze and resolve conflicts but also the multitude of other levels of influence which include organizational/institutional, community, grassroots, etc. Diamond and McDonald (1996) suggest that "repeated acts of political will and courage from many Track One figures will be needed to correct the situation" (p. 30).

Chapter 3: Research Method

Introduction

I have used a case study approach that utilizes a specific case, involving a research study conducted by Gilles Eric Séralini and his colleagues, as a basis for understanding the larger context of agricultural biotechnology. Séralini's research on Monsanto's NK603 genetically modified corn and the herbicide, Roundup, for which NK603 is designed to tolerate, is the central context for this study. Surrounding the publication, retraction and republication of this article are a multitude of systemic public, academic/scientific, corporate and government responses. I gathered and analyzed a comprehensive data set related to this specific case including two interviews with scientists who have conducted extensive research with transgenic crops and glyphosate. I also conducted a basic comparative analysis of how lead (as lead arsenate and leaded gasoline) and DDT were introduced as viable commercial products and what information (based on written government documentation) was used to develop and implement public policy regarding them. The purpose of using these examples as comparison for the current case is to identify possible patterns of knowledge development and public policy regarding research, industry, government and public safety. My working assumption is that there is a lag time between current public policy development and current scientific research—particularly research related to public health (Morris, Wooding and Grant, 2012; Brownson, Kreuter, Arrington and True, 2006). The processes that take place within this lag time seem to reposition public policy from industry-oriented to public health-oriented. This case study compared the current case with those of DDT and lead to

identify a potential pattern of knowledge production-transformation in the lag time between research and public policy implementation.

I chose to use a case study approach to research and analyze this topic because the key elements of my research design lend favorably to a case study methodology more than other methodologies. For example, contrary to strictly historical research, I have selected a contemporary case in which there are living individuals who can contribute to my research data in addition to research based on past events. In researching past and current events, I have integrated documents, archival records and mainstream media rather than rely strictly on survey data with the intent to provide a richer context for a more in-depth understanding of my topic. Although the boundaries of this case can reasonably be defined, this case is situated within a complex system with a multitude of variables that incorporate science, economics and politics that cannot be controlled, and therefore, would not be feasible to design and carry out an experiment (Yin, 2014). A phenomenological approach, however, would be a good alternative for this topic as it would allow those directly involved with the information/knowledge flow an opportunity to voice their experiences. Access to, and participation from, appropriate participants (e.g. scientists, industry representatives, U.S. government representatives, EU Food Safety Authority and EU Commission representatives, as well as WHO representatives), however, would be a challenge and are beyond the scope of my capacity at this time. Because of the complexity inherent within this topic, I have chosen to use case study methodology to help maintain the scope of my project while allowing me to explore a variety of sources that will provide rich, contextually-based data set in a real-world

context. By limiting the scope, especially limiting the number of interviews (particularly from individuals who have personally/professionally experienced the processes that I researched), I inevitably limited the capacity, context, depth and breadth of understanding the topic as a whole. But through the process of in-depth analysis, triangulation and comparative analysis, I hope to compensate, in part, for this shortcoming and offer a credible investigation into the processes of knowledge transformation and, perhaps, illustrate potential change indicators for public policy transitions.

Integrating Analyses

I analyzed the potential for these transitions with what seems to be evolving perceptions of risk vs. benefit. There appears to be a divergence between U.S. and E.U. perceptions of risk taking and precautionary measures in regards to balancing the positive rewards and the negative consequences of new technology, with the U.S. seemingly more willing to take risk and the European Union taking a more precautionary stance (Kogan, winter/spring 2004). Factors that seem to promote this divergence are the criteria that justify cause for concern and, thus, cause for risk-taking or precautionary measures. This is a key reason for me to include a basic comparison/contrast with DDT and lead. I was at first tentative to explicitly include them in this study because I felt it might automatically taint the bio-agriculture industry in a negative light. However, considering the shift in how government policy accepted and promoted DDT and lead initially, as viable industry products, and then later banned or restricted the use of those products, it seems a viable question to ask whether the research and policy trends surrounding the current case are

comparable in terms of how science, industry, and government shape knowledge, policy and regulations.

By focusing on a single case as my primary topic and then comparing it with two other cases (three if one considers the two different applications of lead presented in this study), I initially begin with a comprehensive internal analysis and then include a basic comparative analysis relying mainly on secondary sources with two interviews as primary data from public researchers who have conducted research on transgenic crops and glyphosate. Throughout this process, I maintained a constant effort to appropriately balance and relate emic issues (relevant to policymakers, scientists and industry) to etic issues of public safety (Stake, 1995).

Data Sources

I am highly aware that I am assuming Séralini's research potentially indicates similar early warnings that are illustrated in the lead and DDT cases. To ensure a balanced perspective, I included the perspectives of scientists, industry representatives and government as valid sources for analysis. This information came from scholarly research articles (from academic, independent and industry-supported researchers), industry reports, government documents, and science, academic, industry and government websites. A more thorough explanation of the data types and how I intend to use them in my research can be found in the "Criteria" sections below.

In addition to print media, my research included two email interviews from adult participants who have conducted research on behalf of the government, academia and/or industry that relates to this specific case. In working with human subjects, I respected the

rights and privacy of the interviewees. In requesting interviews, I respected and informed my potential informants that interview participation was voluntary and that they could withdraw from the interview at any time. In respecting the privacy of the participants, I asked for their preference in regards to including information that could personally identify them. From the interview process, I used interview/informant information that was directly relevant to my research and that the participant had given consent for me to use. I presented their information in a way that reflects the original intent and context of meaning so as not to misrepresent the participant's information. As part of ensuring that my interpretations were accurate, I allowed each participant to review and suggest revisions on the text that specifically used their information and identified them personally. I asked if the content accurately reflected their message or if there were any revision suggestions. I received approval with no revision suggestions from one and I received suggestions for revision from the other, which I did and resubmitted to the participant, and subsequently received approval. I have saved the emails and attachments from these two email interviews on a thumb drive, which is stored in a safe location and will be treated as confidential information and I will not share them outside of the immediate context of my written dissertation. Upon approval of my dissertation, I will safely store the emails/thumb-drive, for the IRB required 36-months and then safely dispose of them if the interview participants request it.

Documentary criteria.

There is an extensive amount and variety of print information available from which to analyze existing information regarding this case (as well as DDT and lead) and

the processes of knowledge, policy and regulation creation. To ensure that my data is balanced and representative of the interests of relevant stakeholders (e.g. researchers, industry, and government) I have conscientiously drawn from a wide range of credible sources and, as Yin (2004) suggests, in using a variety of documents, I have "appreciate[d] the differences in perspectives, if not ideologies, represented by the authors of the various types of documents" (p. 156). But it is not only the author's perspective that I have kept in mind, but also the ideologies promoted for the broader stakeholders' interests and I strive to fairly represent their information with integrity. To conserve time and maintain a reasonable scope, I have also followed Stake's (1995) suggestion and purposefully triangulated "only the important data and claims" (p. 112). But what I consider important is subjective; however, I considered the interests of those who might oppose such a claim, in order to better deduce what is academically (and not just personally) important.

The bulk of my information directly relates to the research and policy process of NK603 and glyphosate as it relates to public safety. Although Roundup has been commercially available since the 1970's, most of the research available is on its main ingredient, glyphosate, but when available, I included information that directly related to Roundup and since I will be analyzing this issue as part of a larger system, I also included data related to the development of research design protocols that have been used in testing the safety of NK603, Roundup/glyphosate and related products and the political processes that have been developed to assess the validity of those safety tests. There are certain socio-cultural, socio-political and socio-economic factors that contribute to the

conflict, so I researched key issues such as the EU Precautionary Principle, risk-based policies, cultural, economic and political interests and perceptions, national and international trade policies, patents and intellectual property. I collected data from: **Scholarly books, research and journal articles**.

I used information and articles about recent research studies that have been published (and unpublished) regarding the scientific research and assessments, policies, regulations and perceptions of safety of genetically modified Roundup Ready corn, Roundup/glyphosate and related products. This information came from a multitude of books such as: Business and Environmental Policy: Corporate Interests in the American Political System; Democratizing Global Politics: Discourse Norms, International Regimes and Political Community; International Food Policy Research Institute; Uncertain Risks Regulated. Journals selected for research and articles included Chemical Research in Toxicology; Crop Science Society of America; Entropy; Environment International; Environmental Sciences and Policy; Environmental Sciences Europe; Food and Chemical Toxicology; Global Trade and Customs Journal; International Journal of Environmental Analysis and Chemistry; Journal of Epidemiology and Community Health; Journal of the Royal Society of Medicine; International Journal of Environmental Analysis and Chemistry; Regulatory Toxicology and Pharmacology; Seton Hall Journal of Diplomacy and International Relations; Society of Environmental Analysis and Chemistry and Vermont Law Review. In selecting the books and journals/articles for this research, my criteria required that they were peer reviewed, that they related directly to one or more of the following: the subject of NK603 and/or agricultural biotechnology,

Roundup and/or glyphosate, socio-political, economic or cultural issues that directly relate to NK603/agricultural biotechnology and/or Roundup/glyphosate—either in regards to scientific study, assessment or review, and that, as a whole, the sources represented a balanced representation of relevant stakeholder perspectives from scientists and industry. This data collected, along with Séralini's research study in itself, was integral in observing and analyzing the variety of research available in order to compare with the research that has been used to develop public policy which also helps to illustrate the types of research used as well as how science is validated and knowledge is created and utilized within the realm of Science as well as in the bio-agriculture industry and within U.S. and E.U. agriculture and trade policy and regulation. For my comparative analysis I found existing comprehensive analyses that detail the stages of product and policy development and used them to fill in the blanks as needed to address the specifics of my own research, following the same pattern of investigation as described below.

Websites/databases (e.g. government, international organizations; industry, science forums, agricultural forums, etc.)

In addition to scientific and academic research published in books and scholarly journals, I collected data directly from political and/or industry sources that related to policy making, regulations, product development and marketing of NK603 maize (including subsequent revised or stacked versions)/ agricultural biotechnology crops, Roundup/glyphosate. From the following government and international websites and databases I collected data regarding: safety standards and required safety tests for

genetically modified food crops (particularly NK603 maize); safety standards and safety tests for herbicides (particularly Roundup/glyphosate); current and proposed policies and regulations for NK603 maize, Roundup/glyphosate and related agricultural biotechnology crops and pesticides (e.g. a Congressional Act might generalize genetically engineered crops or pesticides and Agency regulations might specify individual crops and pesticides); communications (e.g. EPA memorandums, industry applications for regulatory approval or non-regulatory status) between industry interests and federal agencies regarding, for example, safety tests, research outcomes, policies and/or regulation of NK603 maize and Roundup/glyphosate; reports from U.S. and European agencies and authorities regarding safety and safety standards for agricultural biotechnology—specifically GMO corn and Roundup/glyphosate; past and current GMO crop statistics of herbicide tolerant corn (of which NK603 is a significant part) and herbicide use of Roundup/glyphosate (within U.S. as well as globally); and educational outreach materials regarding GMO corn and Roundup to see how scientific information evolves from laboratory and safety reports within the context of public policy:

- fda.gov-- for data regarding safety of NK603 maize and pesticide residues for human consumption;
- usda.gov websites—for crop regulations and pesticide residue information, crop statistics, and USDA crop research;
- epa.gov—for data pesticide regulation;
- whitehouse.gov, gov.track—for congressional hearings and executive branch communications;

- gpo.gov—for government publications and public notices;
- nih.gov—for health related research;
- gao.gov—for internal government agency assessments;
- reaganlibrary.archives.gov—for key perceptions from the Executive Branch that was in office when many agricultural biotechnology policies were established;
- National Academies Press—for federal scientific assessments and reports;
- legcounsel.house.gov—for information regarding specific lawsuits;
- bfr.bund.de/en—for information regarding European glyphosate assessment;
- oecd.org—for information regarding international toxicity testing standards and economic objectives for agricultural biotechnology and accompanying pesticides;
- europa.eu, ec.europa.eu, europarl.europa.eu and eur-lex.europa.edu—for information regarding EU policy process and legislation
- efsa.europa.eu and EFSA Journal—for information regarding safety assessments;
- tvnewsroom.consilium.europa.eu—for EU public news releases;
- ey.com—although this is a commercial website, the data I collected was an article written by a former EU Commissioner for Research, Innovation & Science that provides information about EU technology goals;
- iarc.fr/en—for information regarding the 2015 IARC glyphosate assessment;
- European Environment Agency—for information about EU cultural, health and environmental interests;
- glyphosate.eu—for information specifically about glyphosate in the EU;

- Michele-rivasi.eu and ota.fas.org—for information about current European controversial issues;
- who.int and fao.org—for information about past and recent international collaborative assessments of glyphosate

I have also reviewed information from international science-based resources such as the International Service for the Acquisition of Agri-Biotech Applications (isaaa.org) which is a database that offers a comprehensive list of genetically modified crops, their regulatory status according to country, product (event) description, etc. From the industry websites (specifically monsanto.com) I gathered industry perspective to see how scientific information is utilized and presented at the industry level. From science and agricultural forums (e.g. agri-pulse.com and university extension sites), I gained a variety of perspectives regarding what scientists and agricultural stakeholders consider key issues for genetically engineered food crop safety as well as what they consider as sound or faulty science. A key reason for including science and agricultural forums is that this is an outlet that invites relevant stakeholders to share how industry and public policy impacts or influences their interests. It offers a type of feedback that contributes to a type of information loop that may or may not, as the research indicates, influence the current agricultural system.

Interview criteria.

Through purposive sampling, I selected my interview participants based on their experience with bio-agriculture technology and the research that is specifically related to Roundup Ready Corn and/or Roundup. The two interview participants with whom I

chose to communicate directly are both recently retired from government research and/or academic research positions that enabled them to work directly with federal agricultural biotechnology programs and their long-standing careers as public-supported scientists in the fields of microbiology and plant pathology offer a high level of validation in regards to their experience with and expertise in Roundup Ready crops and Roundup/glyphosate safety and safety assessments. Upon my initial investigation into this topic, it seems that the independent and public-supported researcher perspective is least officially documented and, therefore, potentially needs more clarification. Below is a brief description that highlights how the work of these two participants relates to my research topic.

Don M. Huber is a plant pathologist with an active fifty-eight years of experience within the U.S. government and academia holding such positions as: Senior Medical Analyst and Commander in the United States Army Strategic Medical Intelligence; Advisory Board Member for the Congressional Office of Technology Assessment—now the Congressional Research Service and the National Plant Disease Recovery System (NPDRS) –a program designed to meet, in part, the Homeland Security Presidential Directive; associate professor as a cereal pathologist at the University of Idaho; and full/emeritus professor of soil-borne diseases at Purdue University). Perhaps most relevant to my research, however, is Dr. Huber's relationship with the USDA as member and former Chairman of the USDA's Cooperative State Research Education and Extension Services and his 40-year membership with the Department of Defense and USDA-APS National Threat Pathogens Committee. The purpose in detailing Huber's

work experience is to create a sense of credibility, i.e. he is a reputable scientist with extensive experience in the U.S. government and academia. I directly communicated with Dr. Don M. Huber (May 23-June 7, 2016) via email through which he included: a confidential letter that he had sent to the USDA's Secretary of Agriculture, Tom Vilsak; a follow-up letter to the U.K.'s Secretary of State for the Environment, Food and Rural Affairs, Caroline Spelman, MP; a handout generalizing the negative impacts of glyphosate, Roundup and genetically engineered products; and additional information regarding his experiences with the USDA.

Dr. Kremer is recently retired after working with the USDA-ARS for approximately 30 years as a microbiologist—the last (approximately) 17 years of it was dedicated mainly to researching glyphosate interactions with soil and plant (conventional and transgenic) microbiological systems. In 1996, Kremer participated in a collaborative project between the USDA and the University of Missouri that initially focused on the effects of pesticides on soil organisms as well as how to control for a certain pathogen specific to soy. Their research extended to include transgenic soy as it became commercially available. But research outcomes were modest and funding for the project was not renewed. Kremer and one other USDA researcher, however, were able to transition their research on transgenic soy, glyphosate and soil interactions into their existing projects within the USDA. Since then he has published several articles and papers, co-organized a symposium for the 2002 American Society of Agronomy meetings, and presented in several symposia including two in Brazil (in 2005 and 2007) on glyphosate and transgenic crops. Kremer has also been invited to present or work on

special projects for a multitude of agricultural related groups, consulting firms, industry and academic meetings, panels and symposia and edited a 2009 special edition of the European Journal of Agronomy. I selected Dr. Kremer because the length of his career in the USDA and his work with herbicide tolerant crops and glyphosate offer a valuable input regarding knowledge and public policy transitions, within the context of public research and agency support, since the beginning of commercialized herbicide tolerant crops.

In conducting interviews, I prepared a brief set of questions to help initiate and focus the topic and encouraged the participants to share any other relevant information that they considered important. The purpose of getting personal input from interview participants is to incorporate primary research that can be compared and/or contrasted with secondary research. Including peoples' stories also adds an element of verifiability, life and alternative perspectives to the topic. Whether I used secondary sources in my research or included primary information, I verified my data findings through multiple sources. I am highly conscious of my own biases and have been vigilant in checking my assumptions and keeping my mind open to alternative perspectives. My interviews were loosely guided by the following questions that were presented to either or both of the participants (see Appendix C for more details on follow-up questions and the context within which I ask them):

1. How was your research received by the USDA?

2. From your experiences and observations working with the USDA-ARS, what are key factors that influence how USDA decision-makers select and validate knowledge/data for regulatory and policy change?
3. From your perspective, how does the current USDA system (of data selection, collection and use in regards to glyphosate/glyphosate formulations and transgenic crops) impact the USDA's capacity to function as a public agency?
4. How do you envision this system changing?
5. There is a lot of chatter on the mainstream web about a letter that you had sent to the USDA's Tom Vilsack but I couldn't find any official documentation of it. Please let me know if I am overstepping my boundaries, but I was wondering if you really sent one or if the rumor-mill created it. If you did send it, would you be able to tell me what it was about and how Vilsack responded?
6. Have you attempted to communicate your research findings, and subsequent public and political implications, regarding your recent research findings with the USDA (or any other government body) prior to that letter or since that letter, and if so, what was their response?
7. Based on your extensive experience as a publicly supported researcher, how do government regulatory policies for agricultural biotechnology reflect the general state of, and use of, agricultural science and the data generated from it? (How do your recent research discoveries relate to this?)

8. How do you envision a significant positive transformation of the current policy-making, regulatory, and/or agricultural system—i.e. what do you think it will take to shift the balance in the current system?

I emailed my interviewees, introducing myself and the purpose of my research and the purpose of my contacting them. Each participant explicitly invited me to interview him. In seeking participation, I provided written assurance that participation was voluntary and that the interview/communication process would be conducted and information collected would be treated within academic ethical guidelines. I made every effort to preserve the integrity of their contribution and invited them to review any material generated with their specific information, which they did, upon which I sought their verification that I represented them fairly and accurately and asked if they recommended any revisions. One approved the initial draft I sent and the other asked for a few revisions, which I did and resubmitted the draft for his approval, which he then granted.

Inductive and Deductive Category Development

In terms of my overall topic, the overarching theme for this research is the phenomenological process of knowledge transformation as it pertains to science, industry and government bio-agriculture safety testing. I conducted an exhaustive review of the data related to this case (and a brief review of the two comparative analysis examples). As part of the data collecting and analysis process, I read/reviewed the data, making notes in the margins that summarized the content of small portions of the data and highlighted questions that required additional research. This was the beginning and middle of my

coding process as I revisited these codes to clarify vague terms, condense redundancy and streamline main ideas that served as an initial step in developing and connecting relevant categories and themes to my research questions, theories and propositions. From there, I began to link, focus and reduce the various codes into categories and subcategories (Lichtman, 2013). I revised my categories using Philip Mayring's (2000) models (see Appendix 1 and 2) as loose guides for checking my coding to category processes as I inductively developed codes from the data and categories from the codes, making sure that the categories were appropriate for the research questions and, in turn, my research questions were still appropriate for the case. I also used a type of deductive category development as a way to check my theories and proposition. I anticipated key concepts/themes would emerge as I worked through the code to category process. And, as suggested by Lichtman (2013), I limited my concepts/themes in order to refine the focus and depth of my research. The themes I arrived at are as follows:

1. "Developing Standards".
2. "Data Access Restrictions".
3. "Data Gaps".
4. "Perceptions of Safety and Validity".

Chapters four and five maintain the themes in the order presented above. Chapter six uses the same themes, but the order is different so as to present a more fluid narrative. The actual process of collecting and organizing the data was less linear than what I have described above, as I collected and reviewed the data and made my notes, categories and themes evolved and were integrated not only with my research questions, theories and

propositions, but also with my research goals. However, the process was similar to trying to appropriately organize a library in which all of the books contain a similar topic thread but discuss a multitude of issues within that topic that overlap and share qualities that make them difficult to tease apart. In other words, the themes that I finally arrived at sometimes overlap, but they are each distinct enough to hold their own. It was a messy process of back and forth searching, discovery and analysis that finally evolved into a coherent story.

Researcher Role

How this topic was selected and why I chose to research it are important factors in understanding the perspective from which this project has grown. Like many people, I love food. However, about 15 years ago, I had to exclude certain foods from my diet (mainly wheat, rye and barley) in an attempt to correct a thyroid problem, which, after further tests in the following years, it did. Over the years I became more conscientious about the food I, and my family, consumed but my research pursuits were little more than personal exploration. My interest in the topic of agricultural biotechnology and Séralini's case evolved shortly after the initial positive/negative media perspectives were published regarding Séralini's et al (2012) study. Until that point, I was unaware of the extent to which agricultural biotechnology, and herbicide-tolerant corn, had become integrated within the U.S. agricultural system. The outcomes of Séralini's et al (2012) study and the responses from the public, scientists, industry and government in terms of safety, scientific validation and public policy intrigued me enough to not only want to learn more but also to make it the topic of my dissertation. I wanted to learn more about the topic in

general and I wanted to understand the underlying factors that contributed to the conflict and in order to do that, I felt that I needed to understand the context and perspectives from which each of the parties were situating their positions and interests. Therefore, my role as a researcher is one of relativist interpreter with a constructivist view. As Stake (1995) puts it, I was an "agent of new interpretation, new knowledge, but also new illusion" as I collected, interpreted and now present raw and secondary data for my readers (pp. 99-102).

Expected Contributions

The USDA's Office of Communications (March 2003) statement that "[a]gricultural biotechnology is rewriting the rules in several key areas—agricultural policy, industry structure, production and marketing, consumer preference, and world food demand—and public policy is struggling to keep up", invites a significant question: How is this system created and sustained and are there trigger points for change that might give the U.S. government an opportunity to not only "keep up", but perhaps influence how the system operates? Underlying my curiosity about how Séralini's case relates to lead and DDT cases is what seems to be the critical factor of *lag time* between science (knowledge discovery) and mainstream action (which significantly relies on how the original knowledge has been shaped and disseminated). This study has examined the complex interconnected systems that help create and transform food safety policies of a specific biotechnology and has compared them to how lead and DDT policies were transformed (from the researcher to policy development). The resulting analysis found

similarities in scientific validation, policy decisions, public awareness, independent science development and policy change.

Qualitative research is openly interpretative and thus, as stated in Stake (1995), more about developing “assertions” than discovering “findings”. But in order to develop assertions one has to explore (or at least consider) a multitude of possibilities and perspectives—not just our own realities but also those of others as we imagine/perceive them. Becoming so familiar with the multiple elements of a case enables one to better relate the case’s unique qualities with common elements that relate the case to other events (p. 42-44). This, in turn, might invite further investigation into other current policy processes that utilize science (e.g. nutritional pyramids to global warming) to protect public health and industry interests. In terms of conflict analysis and resolution, I hope that my research will make hidden and/or complex relationships and systemic factors and processes more transparent. By making these relationships, factors and processes more transparent, I hope to provide an opportunity to better understand current assumptions and expectations of science and the complex systems within which scientific knowledge is created, transformed and used in regards to agricultural biotechnology public policy. By better understanding current assumptions and expectations, there is a window of opportunity to recognize new perspectives and worldviews. From this understanding, I hope my research provides an inspiration for positive change, whether it is at an individual, institutional or government level.

Chapter 4: Results

Introduction

There are several reasons for conducting this research, the three most important are: 1) corn is a major crop that impacts U.S. and global economies, health and environment, 2) NK603 corn (whether it is grown as a single GE trait or stacked) makes up a significant percentage of corn crop acreage and Roundup is one of the most widely used agricultural herbicides, and 3) the on-going controversy between scientists, government and industry regarding the safety of these products suggests there is a potential red flag in the scientific-industry-government triangle of knowledge production, dissemination and implementation. From the research and analysis, the following themes, listed below, have evolved.

- Developing Standards
- Data Access Restrictions
- Data Gaps
- Perceptions of Safety and Validity

Introducing the U.S. Agricultural System

The federal process of regulating public health and safety in terms of bio-agriculture product consumption is part of a system in which Congress passes laws (Congressional Acts) and Agencies (e.g. FDA, USDA, and EPA) develop regulations meant to help implement and enforce those laws. In other words, the laws provide the outline and the regulations provide the details that make the law actionable. The terms “policy”, “public policy”, “government policy” are often used interchangeably with

"rules and regulations". Policy can be described as an umbrella term that encompasses those laws and regulations. But policy is more than that; it also encompasses the social, moral and economic principles that help influence how these acts and regulations are developed (http://publichealthlawcenter.org/sites/default/files/resources/tclc-fs-laws-policies-regs-commonterms-2015.pdf).

As a way to try to ensure the federal government is operating according to those social, moral and economic principles, the Government Accounting Office (GAO), often called the "congressional watchdog", audits, investigates and analyzes the efficiency and integrity of the U.S. government. The GAO operates as an independent agency headed by the Comptroller General of the U.S., who, according to a 1980 GAO report, is very well-insulated from interest group pressures (Eschwege, Aug. 7, 1980). It is GAO's job to "advise Congress and the heads of executive agencies about ways to make government more efficient, effective, ethical, equitable and responsive" (http://www.gao.gov/about/). (Their reports are included in my research because they offer, to an extent, a relatively neutral government perspective and focus on critical analysis (that is independent of the EPA, USDA and FDA) that can influence organizational and policy change.)

Theme 1: Developing Standards

Cultural Transitions

Until recent decades, agricultural research and development was a public endeavor. Federal funding for a variety of state projects allowed for flexible, local and contextually-based funding that met local needs while offering a high return (~50%) on government investments. As technology transitioned from labor-intensive technologies to

industrial technologies that focused on developing mechanical labor and fertilizer/pesticide technologies, the government has seen financial investment returns of over 100% as agricultural output more than doubled since the 1950's (Wang, Heisey, Schimmelpfennig and Ball, July 2015; Committee on a National Strategy for Biotechnology in Agriculture, 1987). According to an OECD report, in addition to dramatic production increases, labor decreased by approximately 88% and mechanization and herbicides contributed to a fourfold increase in U.S. corn production rates between 1930 and 1980 (Sundquist, Dec. 1989). Sundquist (ibid) suggested that since conventional agricultural techniques had led to such significant yield increases, biotechnology was envisioned as a complementary tool to help advance the potential of agricultural biotechnology.

Prior to the 1970's, the United States Patent and Trademark Office denied permission to patent seeds on the grounds that they are naturally occurring life forms and, therefore, are not patentable. However, the groundwork for new legislation was laid in the early 1970's when a scientist, Ananda Mohan Chakrabarty, tried to patent a lab-created bacterium, arguing that this strain of bacteria was not naturally occurring but rather man-made (https://supreme.justia.com/cases/federal/us/447/303/case.html#311). According to the document, the Chakrabarty case was guided by the 35th U.S. Congress § 101 (based on the writings of Thomas Jefferson), which states, "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title", the question of whether "manufacture" and

"composition of matter" applies to life forms became the central argument (ibid). The document stated that the petitioner in this case raised a precautionary note specifically addressing the question of biotechnology patents and the potential negative consequences if we are unable to fully control the forces our human ingenuity creates (ibid). In addition, according to the document, former Justices Brennan, White, Marshall and Powell expressed concern regarding whether the rights to a manufactured life form should be allowed to be monopolized by an individual and their argument questioned the extent to which the U.S. Constitution, under Article one Section 8 ("To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries"), authorizes individual claim to life forms (https://supreme.justia.com/cases/federal/us/447/303/case.html#311).

In a back-and-forth exchange, according to the author, between court rejection and respondent appeal that lasted from 1972 to 1980, the U.S. Supreme Court deliberated on the semantics of the law (stating that their job was to interpret the existing law and that it was Congress' job to change the law) decided in a five-to-four vote (with Justices Burger, Stewart, Blackmun, Rehnquist, and Stevens assenting) that genetically engineered bacteria was patentable because it was not a product reproducible in nature (i.e. that specific life-form existed from man-made processes). The authors suggested that that particular ruling was a turning point for agricultural biotechnology commerce as numerous patents for bio-engineered seeds and plants were awarded in the following decades, laying the groundwork for a handful of corporations to retain the rights to their

versions of bioengineered seeds and plants (https://supreme.justia.com/cases/federal/us/447/303/case.html).

The National Science and Technology Policy Organization and Priorities Act of 1976 (94th Congress, May 11, 1976) spoke of strengthening the innovative capacities of government, institutions and industry through, in part, "the elimination of needless barriers to scientific and technological innovation" (94th Congress, May 11, 1976). Both the National Science and Technology Policy Organization and Priorities Act of 1976 (ibid) and the Stevenson Wydler Technology Innovation Act of 1980 promoted the integration and interdependence of industry, technological development and government to advance agricultural innovation by fostering connections between institutional research and commercial application. The Stevenson Wydler Technology Innovation Act of 1980 emphasized that industry, technology and innovation "are central to the…economic, environmental, and social well-being of citizens of the United States…[and] would reduce trade deficits, stabilize the dollar, increase productivity gains, increase employment, and stabilize prices (https://legcounsel.house.gov/Comps/Stevenson-wydler%20Technology%20Innovation%20Act%20Of%201980.pdf). Implementing both acts, according to the discussion in the 94th Congressional hearing, would provide the economic security and bridge academic research with commercial applications as the means by which public investment in academia would achieve its tangible returns (94th Congress, May 11, 1976).

By the 1980's the U.S. government began committing a portion of the federal budget to developing agricultural biotechnologies. According to a survey of projects

being funded by the USDA, by 1985 there were 778 bio-agricultural technology projects underway at the time—the majority of which focused on r-DNA technology with approximately $40.5 million—approximately 6% of total USDA expenditures that were allocated for 1984-1985 (GAO, Oct. 1985).

Salomon Wald (1996), the Directorate of the OECD's Science, Technology and Industry, suggested that biotechnology (as a whole science that included pharmaceutical, environmental and agricultural) had the potential to compare with the whole societal permeation that electronic innovation accomplished. Wald (1996), however, also predicted that consumer resistance to agricultural biotechnology would challenge industry marketability and that agricultural biotechnology companies, as a reaction to this resistance, might exaggerate "regulatory hurdles that have been used as instruments of delay", without recognizing or acknowledging that underlying these barriers is the "absence of a genuine demand pull for new biotechnology-derived foodstuffs" (p.11).

Wald (1996) suggested agricultural biotechnology marketing strategies to boost its public acceptance: as a product of convenience [marketing simple solutions that solve a real problem]; as a nutritional product [promise of specific nutritional qualities]; as a healthy and safe product [substantially equivalent to "normal" product]; or as an ecologically sound solution [reduce pesticide use and tillage]. Agricultural biotechnology was also expected to meet future climate change needs and become an essential tool to address increased environmental degradation (p. 11). Wald (1996) noted that "[b]iotechnology can help to meet these needs, but is not the only, and often not the most readily accepted, tool for developing new foods to meet these public demands and hopes"

(p. 11). Wald (1996) recognized that, although at the time the agricultural market was saturated, the perceived need for agricultural biotechnology was expected to increase as an answer to meeting food supply needs for a growing global population (in a mid to long-term projection). However, in regards to pesticide application, agricultural biotechnology was expected to replace conventional techniques (Sundquist, Dec. 1989).

According to NAS and OECD and the USDA, although herbicide tolerant crop acreage has increased exponentially compared to its conventional counterparts, there is no conclusive evidence of a subsequent increase in crop yields (National Academies of Sciences, Engineering and Medicine, 2016; OECD, 2016; Fernandez-Cornejo, Wechsler, Livingston and Mitchell, June 2014). In the National Research Council's (NRC) (2014) review of USDA agriculture and research, they stated that:

> A progressive slowing of U.S. (and global) agricultural productivity growth from the historically high growth rates of the 1960s, 1970s, and 1980s has been observed in the last 20 years (Table 2-2). In every region of the United States, average annual multifactor productivity growth rates for the more recent period, 1990–2007, were significantly lower than in the previous period, 1949–1990. (ibid)

A recent study from the U.S. National Academy of Sciences, Engineering and Medicine was tasked with analyzing the safety of current and future genetically modified crops and, according to a New York Times article, indicated that although genetically engineered crops have, in some cases, provided economic benefit for farmers, the overall national yield averages are relatively insignificant, bringing into question the ideology

that agricultural biotechnology was “essential…to feeding the world as the population grows” (http://www.nytimes.com/2016/05/18/business/genetically-engineered-crops-are-safe-analysis-finds.html?_r=1).

According to Davies, (Feb. 17, 2016), since the USDA, in 2000, approved NK603 for non-regulated status, single-trait herbicide tolerant corn grown in the U.S. has doubled and stacked trait corn (many of which include glyphosate tolerance) has increased from 1% to 77%. In addition, since 1990, the emphasis on innovative agricultural biotechnologies has simplified rather than diversified the overall U.S. agricultural production, limiting the majority of U.S. crop commodity crops to corn, soy, wheat and cotton which, since 1990 has grown from 218 million to 242 million acres (https://www.ers.usda.gov/topics/crops/). According to an opinion statement of the European Economic and Social Committee,

> One key objective of EU agricultural policy must be to maintain diversified agricultural production and promote it across the EU. Maintaining the rich diversity of high quality food from different rural areas throughout the Union for EU citizens will provide the right strategic solution for the EU food policy. (Krauze, 2011)

On a similar note, the EC (June 8, 2016), along with EU High Representatives for Foreign Affairs and Security police, published a statement that underscores EU value on culture in a press release titled: “A new strategy to put culture at the heart of EU international relations”. Within their statement, “EU High Representative and Vice-President Federica Modherini said: ‘Culture has to be part and parcel of our foreign

policy...It can also be an engine for economic and social development…[C]ultural diplomacy must be at the core of our relationship with today's world'" (EC, June 8, 2016). While the press release integrated cultural objectives beyond agricultural trade relations, the overall message reflects a key factor in EU resistance to GMO market and crop integration (ibid). But the WTO recently proposed a new trade stipulation that prohibits the EU's capacity to refuse GMO's on the basis of health or environmental hazard (https://www.wto.org/english/tratop_e/dispu_e/cases_e/ds291_e.htm). In response, the EU, in 2015, gave permission to its member states to ban GM crop cultivation (but not importation) on the basis of "socioeconomic impacts or other compelling grounds not linked to risks to human health or the environment" (EPRS, July 3, 2015).

Some proponents of agricultural biotechnology frame E.U.'s precautionary approach in competitive terms when comparing the E.U. to the U.S. For example, the European Commissioner for Research, Innovation and Science, Geoghegan-Quinn (2014), described the E.U. as "lagging behind" and needing a solid "action plan" to ensure a "level playing field" in order to "retain our competitiveness" (p. 1). According to Wirth, (2012-2013), although the EU is not opposed to biotechnology and has been an active participant in developing strategies and action plans to promote and advance the development of biotechnology (agriculture included), the overall drive to replace current agricultural systems and permeate society with this new technology, does not match that of the U.S. According to the European Economic and Social Committee, "[a]griculture has traditionally been a sticking point in the negotiations because most countries defend

their own production on the grounds of basic security" (http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52008AE1668, sect. 3.3.3). Le Menestrel and Rode (2013) note that from an international trade perspective, it seems that many socio-cultural and environmental risks are generally beyond the parameters for internal, industry-level decision-making processes except when those risks threaten the security of 'legal fortitude, the non-restrictive state of regulatory conditions, or reputational advantages'. In other words, the nature of international crop commodities trading is responsive to self-protective measures of legal rights, regulatory freedom and marketing advantages.

The Director General of the E.C. Health and Consumer Protection Directorate, in a comparative case study analysis between risk management policies between the EU and the US, mentioned a number of limits to science in regards to public policy" (Coleman, Jan. 11-12, 2002). Coleman (Jan. 11-12, 2002) went on to detail those limits as factors of time, perceptions of validity, and subjectivity, stating specifically that it takes time to "generate the experience, the raw data, which will permit reliable scientific analysis of innovation to be done"; that there is "still unsettled debate concerning the difficulties of determining what, in a given field at a given time, science or "sound science" actually is"; and that there is the "virtually unavoidable… introduction [of] subjective elements of value judgement in the course of planning, conducting and evaluating the process of scientific investigations" as in toxicological studies where, for example:

> the choice of the test animal species, the strain, the sex, the age of the animals, the route and the duration of the administration of the test substance, the length of the observation period, the choice of the test parameters to be evaluated and many

other factor can profoundly influence indeed determine, the outcome of the test" (Coleman, Jan. 11-12, 2002, p. 3).

Cohen (1996) states that time is one of culture's most "insidious" features as it impacts one's "judgment of the right moment for the performance of a given action; and…the sense of the appropriate rate of progress or transition from one move to the next" (p.119). Concern within the EU government regarding the safety of glyphosate and, particularly, its accompanying adjuvants (including POEAs) has EU officials discussing patent law revisions, and regulatory policy changes (EC, Council of the European Union, March, 2016). The 2016 U.S. National Academies of Sciences, Engineering and Medicine study emphasized that "[t]here is an indisputable case for regulation to be informed by accurate scientific information, but history makes clear that solely "science-based regulation" is rare and not necessarily desirable…[and] decisions about how to govern new crops needs to be made by societies" (National Academies of Sciences, Engineering and Medicine, 2016, p.x).

Defining Roles in the U.S.

In 1983, the Committee for Scientific and Technological Policy met to discuss the efficacy of biotechnology (Committee on Science and Technology, Feb. 3, 1983). The Committee discussed how federal government (after WWII) became the parent supporter of scientific research in the U.S., operating under the assumption that "science had become a significant factor in maintaining a strong defense and a strong economy, and also in recognition of the fact that, at the funding level required, no source other than the government could assume that responsibility" (Committee on Science and Technology,

Feb. 3, 1983, p. 7). But regardless of the intentions, the committee recognized that more funding than the government could afford was needed, that academic research was consistently underfunded, and institutions were ill-equipped to meet the needs of industry (Committee on Science and Technology, Feb. 3, 1983). It might be useful to note that the goal of the Executive Branch, at the time, was "to nurture the strength and vitality of the American people by reducing the burdensome, intrusive role of the Federal Government" (Reagan, 1981). President Reagan stated: "It is our basic belief that only by reducing the growth of government can we increase the growth of the economy"" (ibid). The sentiments of minimizing financial and regulatory burden on private industry were not only priority for the U.S., but also echoed in the OECD (OECD, Sept. 1982). Inviting biotechnology industry stakeholders, from various fields, to take part in developing regulatory processes was a government strategy to create a more efficient system for industry and government to get the most out of biotechnology benefits while striving to minimize the risks (Committee on Energy and Commerce, Dec. 18, 1985, https://babel.hathitrust.org/cgi/imgsrv/image?id=umn.31951d00283126s;seq=7;width=8501985).

Cooperation between industry and government extended to the agencies (EPA, USDA and FDA). According to the EPA, the goal of the EPA—to "establish and enforce environmental standards consistent with national environmental goals" — plays a significant role in protecting public health and the environment (https://www.epa.gov/history/origins-epa; https://archive.epa.gov/epa/aboutepa/ash-council-memo.html). But, according to the 1970 Ash Council Memo, from the start, it

was known that the EPA would be operating “on the horns of a dilemma” as an advocate and enforcer for public and environmental health in the face of the economic progress that matches, and perhaps also drives, our accustomed or desired standard of living. As stated in the Ash Council Memo for President Nixon which initially laid out the rationale and structure for the EPA, a

> [s]ound environmental administration must reconcile divergent interests and serve the total public constituency. It must appreciate and take fully into account competing social and economic claims… [in order to] sustain a well-articulated attack on the practices which debase the air we breathe, the water we drink and the land that grows our food. (https://www.epa.gov/aboutepa/ash-council-memo.html)

In regards to agricultural biotechnology, EPA regulations state that the majority of the EPA’s authority is in setting and enforcing pesticide standards that are granted under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) which charges the EPA with assuring that each pesticide registered will not cause:

> (1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under section 408 of the Federal Food, Drug, and Cosmetic Act " (https://www.epa.gov/laws-regulations/summary-federal-insecticide-fungicide-and-rodenticide-act).

By the 1980's however, federal funding had been significantly cut back from EPA applied research budget, restricting their capacity to develop and maintain applicable (and competitive) bio-technological research that could provide a useful knowledge background in their assessments (Committee on Science and Technology, Feb. 3, 1983). Coincidentally, according to multiple sources, in addition to regulating pesticides, the EPA had proposed, in 1983, to regulate agricultural biotechnology under the authority of the Toxic Substances Control Act but was quickly challenged (in 1984) by a Congressional Office of Technology Assessment report that suggested another solution was necessary to ensure the preeminence of U.S. global leadership in biotechnology. In general, the U.S. government recognized the need for federal oversight and through a series of committee meetings and congressional hearings, devised a plan to address those concerns more effectively through intergovernmental coordinated regulation and oversight. The response of the Executive branch (at the end of 1984), according to the sources, was to reallocate regulatory responsibility for agricultural biotechnology with the "Coordinated Framework for the Regulation of Biotechnology" (Hilts, Aug. 9, 1983; Office of Technology Assessment, Jan. 1984; OSTP, Dec. 31, 1984). The Coordinated Framework for Regulation of Biotechnology policy was adopted in 1985 which delegated responsibilities between various federal departments, programs and agencies (Sheingate, Apr. 2006; OECD, Sept. 1982). According to a GAO (Mar. 1986) report, the Executive Branch's Office of Science and Technology Policy (OSTP) held the authority and obligation to help develop and manage federal biotechnology programs. But within a year after the Coordinated Framework was implemented, it became evident that the

overall process of delegated authorities was unclear and interagency/ intergovernmental coordinated responsibilities needed to be more thoroughly detailed, particularly for the USDA (GAO, Mar. 1986).

According to a GAO (Mar. 1986) report, APHIS, in addition to avoiding overstepping authoritative boundaries with OSTP, was at first tentative in making authoritative decisions and/or creating their own regulatory policies that might needlessly stifle innovation. In addition to role confusion and disorganization, public resistance to gene technology had led to public lawsuits against the government, highlighting the tensions between diverging ideologies of the government's risk-based policies and the public's call for precaution and making the USDA hesitant to act (GAO, Mar. 1986). Overall, the GAO, at the time, indicated that until the USDA developed an effective and efficient organizational structure that clearly outlined procedures, delegated responsibilities, and defined authority, it would be incapable of managing and overseeing current and future biotechnology research and field trial approvals (GAO, Mar. 1986). As a means to clarify its role and "[t]o strengthen its relationship with industry, APHIS broadened participation of affected groups in developing regulations through such approaches as negotiated rulemaking, which involved stakeholders in the early stages of drafting new regulations" and by 1986, APHIS (and industry) had become central in determining the regulatory status of genetically engineered crops in terms of whether (or to what extent) they posed as a plant pest risk (https://www.aphis.usda.gov/about_aphis/downloads/40_Year_Retrospective.pdf).

Shortly after the GAO (Mar. 1986) review, the White House's recently created

Biotechnology Science Coordinating Committee announced its decision regarding biotechnology, stating that "[t]he manufacture of food…and pesticides will be reviewed by FDA, USDA, and EPA in essentially the same manner for safety and efficacy as products obtained by other techniques" (OSTP, June 26, 1986, p. 6). Accordingly, the FDA regulates genetically modified food through the food additive provision, in which the FDA regulates general food safety from a post-market position, and the general safety provisions of the Federal Food Drug and Cosmetic Act, which allows the FDA to determine if an added ingredient is "generally recognized as safe" (GRAS). According to the FDA (Oct. 30, 2015), it is the "responsibility [of the manufacturers] to determine that their products meet the general safety standards…labeling requirements and to the extent the food additive provisions apply, to make sure that they are in compliance with those as well" (p. 68-69). In 1997, the FDA implemented a "premarket consultation process" that allows manufacturers an opportunity to (voluntarily) discuss with the FDA the safety, nutrition, and labeling requirements of their products (FDA, Oct. 30, 2015). In addition to the FDA's role in post-market food safety, it is also responsible for ensuring that the chemical pesticide residues in and on post-market food is within regulatory limits. The FDA developed the Total Diet Study (TDS), which analyzes approximately 280 "table ready" products most commonly used in U.S. diets not only for pesticide residue, but also other chemicals, toxins and nutrient levels (e.g. checking manufacturer data for nutritional labeling accuracy on packaged goods—nutritional labeling for fresh produce, however, is voluntary) (http://www.fda.gov/Food/FoodScienceResearch/TotalDietStudy/ucm184232.htm).

After the EPA's proposal to regulate agricultural biotechnology was challenged and rejected with the implementation of the Coordinated Framework, the EPA, pursued with a proposal that under the TSCA the EPA had authority to assess and regulate new microbial substances (which would include certain substances used in r-DNA research) (EPA, Sept. 1, 1994). This proposal was never set forth as a rule and the EPA's role with biotechnology remained limited to assessing and regulating pesticides and chemicals. (EPA, Sept.1, 1994). According to the OSTP (June 26, 1986), "…future scientific developments will lead to further refinement", suggesting that "regulatory regimens could be modified [as they had been in the past] to reflect a more complete understanding of the potential risks involved", meaning that existing regulatory processes for conventional agriculture could be used for transgenic agriculture and modified to address specific risk factors (p. 4).

According to the EPA, from the start, and continuing after the implementation of the Coordinated Framework, one the EPA's major roles was to "review…pesticide formulations for efficacy and hazard" and that a key method used to accomplish that goal was to analyze "all scientific data on the pesticide and develop comprehensive risk assessments that examine the potential effects of the product or ingredient on the human population and environment" in order to appropriately set standards for pesticide registration and regulation (https://www.epa.gov/aboutepa/epa-order-11102; https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/assessing-human-health-risk-pesticides; https://www.epa.gov/pesticide-registration/about-pesticide-registration). Part of that regulation extends to advising the USDA on which pesticides

are recommended for residue testing. The USDA operates the Pesticide Data Program in which samples of certain fruits, vegetables, grains and legumes are selected from various grocery/distribution outlets across the U.S. (USDA, Apr. 1994). The USDA then tests these foods for pesticide residue levels, using various methods that involve more science than I am capable of explaining. The USDA claims that "[t]he Pesticide Data Program (PDP)…produces the most comprehensive pesticide residue database in the U.S." (USDA, https://www.ams.usda.gov/datasets/pdp).

According to a GAO report, the 1996 Food Quality Protection Act was developed in recognition that as science evolves and new information becomes available, certain chemicals might need to be registered and regulated differently. Under this act, the EPA would be required to reassess each pesticide (every fifteen years) as a means of maintaining registration and regulatory standards that are based on the best available science (http://www.gao.gov/assets/90/85152.pdf). To help expedite the EPA's assessment process, the GAO (1986) recommended that Congress change the pesticide laws to require that industry provide all required data for EPA assessment, self-certify and self-regulate their products according to EPA guidelines and standards. The EPA responded that it was in agreement, to a certain extent, with that proposal as they had, in the early 1980's, conducted a pilot test allowing industry registrants to evaluate their own data, identify gaps and, basically, help develop registration standards. However, according to EPA's response, the discrepancy between EPA and industry expectations on what was considered necessary data was disappointing and demonstrated the need for the

EPA to develop specific, comprehensive criteria and standardized guidelines that effectively covered public and environmental health concerns (ibid).

Since the beginning stages of agricultural biotechnology development in the U.S., industry representatives have worked closely with the Executive branch, including the EPA, USDA and FDA creating regulatory procedures and policies for agricultural biotechnology. In contrast, Dr. Kremer noted that "one of the main themes of [USDA] ARS policy is that we, as scientists, conduct research only—we do not make any recommendations for regulatory or policy issues…" (personal communication, June 2, 2016). (This theme topic was raised by other scientists, who were working on nanoparticle technology, who emphasized that "there are deep differences between science and policy, the line between policy-relevant and policy-prescriptive science is under continual negotiation, and there is no uniquely 'objective' way of characterizing facts") (Jamieson, Oreskes and Oppenheimer, Jan. 2015). According to Kremer, even if a policy is directly related to the results of a scientist's work, the USDA-ARS prohibits them from suggesting regulatory or policy changes (personal communication, June 2, 2016).

Henry Miller, had worked in the mid-1970's, for three years, helping the U.S. National Health Institute refine emerging r-DNA techniques and later worked various positions within the FDA from 1979-1994 on biotechnology policy development in such positions as Special Assistant to the FDA Commissioner and founding director of the FDA's Office of Biotechnology and is currently a research fellow at Stanford University's Hoover Institution, focusing his research on science, government, federal

and international regulatory processes and biotechnology (http://www.hoover.org/profiles/henry-i-miller). Miller was quoted in a 2001 New York Times article referencing the relationship between industry and federal agencies: "In this area, the U.S. government agencies have done exactly what big agribusiness has asked them to do and told them to do" (http://www.nytimes.com/2001/01/25/business/25FOOD.html?pagewanted=all). In addition to the bio-agricultural industry interests in the FDA, the bio-pharmaceutical industry emphasized the importance of public trust and how the FDA could provide a level of consumer confidence not easily achieved through industry marketing alone. According to Stone (2002), the pharmaceutical industry had been hindered by the slow and costly FDA regulatory approval process. However, when Congress, in 1995, proposed to privatize several FDA functions, the pharmaceutical industry supported the FDA because "without the seal of government approval for its drugs, the industry would lose the 'world's confidence in the superiority of American drugs' and the public's confidence in the superiority of American drugs" (p. 5). Representatives of the pharmaceutical industry were quoted in Stone (2002), stating: "We are for a strong F.D.A. They are our credibility" (p. 5).

Defining Roles in the E.U.

Reflective of the surging glyphosate-tolerant crop research and field testing in the 1990's, in 1993, over a dozen chemical and agricultural biotechnology companies initially notified the European Commission of their interest in incorporating glyphosate as a plant protection product in the Directive 91/414/EEC. In 1995, they divided into task

forces (indicating a level of international industry cooperation) and submitted their dossiers (within two weeks of each other) to the EU Rapporteur Member State (Germany), which reviewed the dossiers and submitted a draft report to the EFSA (Health & Consumer Protection Directorate-General, Jan. 21, 2002). The EFSA reviewed the draft report (and assessed industry materials if necessary) and, upon approval, passed them on to the European Commission for a final decision (http://ec.europa.eu/food/plant/pesticides/approval_active_substances/index_en.htm).

The EFSA evolved (in 2002), in part, as a response to address food safety and public health concerns following a widespread outbreak of Bovine Spongiform Encephalopathy (BSE)—mad cow disease—that had started in the U.K. in the 1980's and spread throughout parts of Europe, the U.S. and other parts of the world (http://www.cfsph.iastate.edu/Factsheets/pdfs/bovine_spongiform_encephalopathy.pdf). According to the EU, the EFSA plays a key role in the approval process for transgenic crops and chemical pesticides. The Committee on the Environment, Public Health and Food Safety, issued an annex to the Committee on Budgetary Control that was voted favorably and defined the purpose for the EFSA to be:

> the provision of independent scientific advice on matters with a direct or indirect impact on food safety, the conduct of risk assessments to provide Union institutions, Member States and policy-making bodies with a sound scientific basis for defining policy-driven legislative or regulatory measures and the collection and analysis of scientific data.

http://www.europarl.europa.eu/sides/getDoc.do?type=REPORT&reference=A7-2012-0106&language=EN&mode=XML.

Other International Collaborations

In addition to U.S. federal government and the E.U., pesticide and/or GMO safety, the World Health Organization (WHO) often works in conjunction with the U.N.'s Food and Agriculture Organization, among other projects, "for the purpose of harmonizing the requirements and the risk assessment on the pesticide residues" (http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmpr/en/). And IARC is the World Health Organization's International Agency for Research on Cancer and their mission is to foster international cooperation in cancer research, part of which included a recent assessment of glyphosate and glyphosate formulations as part of a comprehensive review of a multitude of currently marketed chemicals (https://www.iarc.fr/en/about/index.php).

Prior to the recent IARC review, the USDA emphasized that corn is a major international trade commodity for the U.S. and most of that corn is genetically engineered, therefore, protecting the economic viability of such a crop "means that working with our trading partners is critical to help them understand the technical aspects of new products and how we have determined that they meet our high safety standards, to open up new markets, and to ensure that our products are treated fairly in the global marketplace" (http://www.usda.gov/wps/portal/usda/usdahome?navid=BIOTECH).

As a response to the global integration of new information technologies, the World Trade Organization (WTO) originally formed in 1995 and by 2000-2001 was

preparing for a new global agricultural biotechnology market integration. A multitude of countries joined as members, the U.S. and E.U. (as representative of E.U. member countries) included, in a collaborative effort to liberalize trade through minimizing trade barriers and providing a forum in which to resolve trade disputes as a means to harmonize commodity standards and streamline international trade between member nations (https://www.wto.org/english/thewto_e/whatis_e/inbrief_e/inbr01_e.htm; https://www.wto.org/english/thewto_e/whatis_e/tif_e/fact1_e.htm).

Harmonizing Roundup/Glyphosate

The data for which the industry applicants were required to submit with the dossiers for glyphosate regulatory approval in Europe was similar to what was required in the U.S. (e.g. detailed chemical description/property identification, environmental fate, eco- and mammalian toxicology, and residue analysis) (http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1438). According to the EPA, under guidance from FIFRA and the National Research Council, the EPA developed a system to streamline registration and re-registration by adopting a four-part assessment process to identify potential hazards, determine toxicity thresholds, analyze exposure levels and conduct risk assessments. As part of the EPA's goal to create an integrated approach to assessing the systemic effects of each chemical they proposed finding a "common mechanism of toxicity" in order to create chemical groups that would help streamline the process. With such a wide array of pesticides on the market, the cumulative impact of pesticides with a "common mechanism of toxicity" had become a

prominent concern to which the EPA was required to address under the authority of the Food Quality Protection Act (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/overview-risk-assessment-pesticide-program). In addition, the EPA also developed the "Integrated Risk Information System" (IRIS) which mainly operates under the legislative guidance of the Toxic Substances and Control Act, (i.e. non-pesticide substances) (https://www.epa.gov/iris). The EPA, in response to the GAO's suggestion, agreed that with appropriate guidance materials, complete data-sets from industry-led studies could help accelerate the registration process (GAO, 1986).

Throughout the 1980's and 1990's, the OECD had also been working towards harmonizing toxicity test guidelines across member country borders by developing standard test designs and procedures for a multitude of toxicity measurements. U.S. federal agencies coordinated in this effort, along with international "regulatory authorities and industry associations to promote harmonization of regulatory requirements" (FDA, Mar. 1, 1994). Such harmonization of internationally agreed upon protocols could help streamline trade and regulatory processes within and between member (and non-member) countries.

According to the EFSA (2015), "[r]egarding carcinogenicity, the EFSA assessment focused on the pesticide active substance and considered in a weight of evidence all available information" (p.2). Such conclusions are based on criteria set forth in EC regulation No 1272/2008 and although this is a 1355-page document that, I admit, I did not examine in its entirety, it seems that article 30 sets precedence for the persistent

conclusions of safety based on tests using the active ingredient rather than the whole formulation:

> Testing that is carried out for the sole purpose of this Regulation should be carried out on the substance or mixture in the form(s) or physical state(s) in which the substance or mixture is placed on the market and in which it can reasonably be expected to be used. It should, however, be possible to use, for the purpose of this Regulation, the results of tests that are carried out to comply with other regulatory requirements, including those laid down by third countries, even if the tests were not carried out on the substance or mixture in the form(s) or physical state(s) in which it is placed on the market and in which it can reasonably be expected to be used.
>
> (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:en:PDF)

Changes to EC 1272/2008 include amendment EC 1907/2006 (which outlines EU's position on the Registration Evaluation Authorization and Restriction of Chemicals—REACH) in which the first article (among many) was amended in 2008 from:

> This Regulation should ensure a high level of protection of human health and the environment as well as the free movement of substances, on their own, in mixtures and in articles, while enhancing competitiveness and innovation. *This Regulation should also promote the development of alternative methods for the assessment of hazards of substances*. (emphasis added)

to this: “This Regulation should ensure a high level of protection of human health and the environment as well as the free movement of chemical substances, mixtures and certain specific articles, while enhancing competitiveness and innovation” http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:en:PDF.

While OECD toxicity testing guidelines focused on standardizing animal testing methodology, the National Research Council has been developing, in coordination with other groups of scientists, new technology and methods using human cells and computers, partly because animal testing is useful to an extent, but its accuracy in determining how a substance will affect humans is limited and the time and resources to conduct such tests are costly. Tox21 was established in 2008 as the collaboration between the EPA, FDA and NIH to actively develop this new methodology to replace the need for animal testing and (hopefully) produce more accurate results. (NIH, Feb. 14, 2008; http://www.pcrm.org/research/animaltestalt/chemtesting/chemical-testing-basics-toxicity-testing).

Harmonizing NK603 (GMO’s)

Within the E.U., there are three main pieces of legislation regarding genetically modified food, feed and cultivation. Directive 2001/18/EC legislates GE crop cultivation and it was amended by Directive 2015/412, to allow member states to opt out, or ban, GE crop cultivation on the basis of “agricultural or environmental policy objectives, socioeconomic impacts or other compelling grounds not linked to risks to human health or the environment” (EPRS, Oct. 19, 2015, p.3). The second piece of legislation is (EC) 1829/2003 which covers GE food and feed and (EC) 1830/2003 covers GE food and feed

labeling. However, within these three pieces of legislation are a multitude of amendments and revisions. Overall, NK603 is encompassed by the following EC Regulations: EC 2001/18; EC 1829/2003; EC 178/2002; EC 1830/2003; 1801/2001; 2283/2015, etc. (i.e. a multitude of regulations impact the policy-making process for NK603) (see Appendix 9 for a list of regulations related to NK603). Moving a pesticide or GMO product from initial petition to final approval can take approximately three to five years (See Appendix 9 for a list of legislative amendments pertaining to GMO's) (http://ec.europa.eu/food/plant/pesticides/approval_active_substances/index_en.htm). For GMO approval, an applicant (company/manufacturer) submits an application and required product-related data to the Competent Authority (CA) of the country in which the company intends to first market their product. In the case of NK603, Spain was the initial CA. The CA reviews the applicant's dossier, (which includes a product description, environmental assessments, toxicology assessments, labeling and detection methods) and if approved, submits the application and submission materials to the EFSA who then reviews the dossier and provides the European Commission with an opinion. The EC considers the EFSA's opinion and each member country (represented by the Standing Committee on the Food Chain and Animal Health) votes whether to grant authorization or reject it. If the EC Standing Committee cannot reach a majority consensus, it gets passed to the European Council of Ministers. If the Council does not make a decision within a specified timeframe or obtain a qualified majority vote, then it returns to the Commission who then adopts the decision (http://europa.eu/rapid/press-release_MEMO-07-117_en.htm).

In the U.S., GMO's are less regulated. The USDA has the authority to assess and regulate plants, including transgenic plants that are considered pests or pose potential harm to other plants or beneficial insects. If a petitioner provides data demonstrating that their proposed crop line is not a "plant pest", then APHIS has the authority to approve field trials and/or deregulate it. By the mid-1990's, APHIS established a rule simplifying GMO crop regulation by further aligning most GMO crops with conventional requirements (APHIS, Apr. 24, 1997). Unless a "food…contains any added deleterious substance which 'may render it injurious to health'", the FDA established a pre-market consultation process and maintained post-product authority in regulating food safety (quoted in Frisbie, Apr. 1936, p.372). Consultations review any potential health concerns or additional clarification needed to ensure the product does not pose public health risk. The FDA considers these voluntary consultations "prudent practice" for businesses to address potential issues early in the process and to demonstrate participatory effort in the FDA's system of regulatory compliance (FDA, May 29, 1992).

According to the FDA, the 1980's signaled the beginning stages of public policy and regulatory development for biotechnology as the U.S. government promoted biotechnological innovation as a key to economic, political, food and even more broadly, cultural security (http://www.fda.gov/downloads/newsevents/meetingsconferencesworkshops/ucm477576.pdf. According to an OECD document (https://www.oecd.org/sti/sci-tech/24508541.pdf), by 1982, international biotechnology patent policies were in various stages from one country to the next and in order to streamline trade it recognized that a more harmonized

patent system between countries was necessary to promote consistent protection for patent holders within global interactions. According to Sheingate (Apr. 2006), by 1986 the U.S. had already determined (unofficially) that further studies that focus on the distinction between transgenic and conventional agricultural biological/microbiological processes were not a priority and a focus on the product rather than the process would not only reduce regulatory responsibility of government and unnecessary burden on industry, but it would promote agricultural biotechnology as a substantially equivalent comparison to traditional crops. In 1993, the OECD adopted the FDA's "generally recognized as safe" (GRAS) policy as well as the U.S. concept of substantial equivalence (https://stats.oecd.org/glossary/detail.asp?ID=2604). Qualifying genetically engineered foods as essentially the same as the consumer-approved conventional foods, according to the OECD, has been recently reiterated as a basis for minimizing trade barriers between OECD member and non-member nations (OECD, Apr. 3, 2015). U.S. federal agencies coordinated in this effort, along with international "regulatory authorities and industry associations to promote harmonization of regulatory requirements" (FDA, Mar. 1, 1994). By 2007, biotechnology had explicitly become the agricultural crop system of U.S. national priority (Homeland Security, USDA, FDA., May 7, 2007, p. 4).

Theme 2: Data Access Restrictions

Protecting Innovation: Benefits and Barriers

In petitioning for pesticide registration approval, the EPA clarified that companies submitting formulations for registrations (or re-registration) must provide the EPA with a complete list of the formulation's active and "other ingredients"

(https://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-15-submitting-data-and-confidential#claims). In order to protect a company's trade secrets (i.e. patent and intellectual property rights) when government reviews are published and made available to the public, the "other ingredients" are often replaced with the initials "CBI" (i.e. confidential business information). Confidential business information includes:

> information that discloses manufacturing or quality control processes (FIFRA 10(d)(1)(A)); information that discloses methods for testing and measuring the quantity of deliberately added inert ingredients (FIFRA 10(d)(1)(B)); and information that discloses the identity or percentage quantity of deliberately added inert ingredients (FIFRA 10(d)(1)(C)). (ibid)

Other means of protecting confidential information in government documents was evidenced in blacked out sections of data that was, presumably, proprietary. In my research, I came across several EPA memos about Roundup and glyphosate assessments in which certain sections, including inert ingredient information, had been blacked out (see Appendix Ea for examples of redacted material). Confidentiality extends across national borders as well. For example, in regards to assessing the safety of glyphosate in the EU, Portier et al (Nov. 27, 2015) reasoned that the EFSA's "use of confidential data submitted to the BfR makes it impossible for any scientist not associated with BfR to review this conclusion with scientific confidence" (pp. 5-6). (Note: BfR, "Bundesinstitut für Risikobewertung", was commissioned in 2015 by Germany to re-assess glyphosate—see below for further discussion.) In the U.S., the Office of Management and Budget

(2002) “Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies” illustrated the balance between the level of transparency needed to gain and maintain public trust and the degree of protection needed to maintain industry proprietary confidentiality. Within these guidelines, according to the OMB, Agencies are given discretionary authority to determine the appropriate data requirements and scientific rigor required to adequately assess industry products while protecting proprietary information (ibid). The guidelines distinguish agency-disseminated scientific data (i.e. official viewpoint of the agency) from data published by a Federally employed researcher (unofficial viewpoint of the researcher), noting also that a Federally employed researcher wishing to publish their findings should include “an appropriate disclaimer in the publication or speech to the effect that the “views are mine, and do not necessarily reflect the view” of the agency (ibid, p. 8454). In terms of peer review, the OMB guidelines generally agree that “peer review is clearly valuable” but “additional quality checks…are appropriate” particularly when a research topic or content contains “influential” information that, if disseminated, “will have or does have a clear and substantial impact on important public policies or important private sector decisions” (Office of Management and Budget, 2002, p. 8455). What is defined as “influential” is dependent upon the interpretation of the agency (ibid).

Dr. Kremer, recently retired from the USDA, noted that within the last 10 years, USDA-ARS researchers have been increasingly prohibited from making opinion statements and prohibited from discussing “anything other than the facts relative to your research and the discussion had to be based on information already approved and

published" (Kremer, personal communication, June 2, 2016). Kremer stated that, in regards to the USDA's support for his research, the USDA was, until about 2009, quite supportive, approving his projects, publications and presentations with minimal revision. In addition, the agency encouraged their scientists to talk to the public about their research. But he began to notice a shift in policy that restricted the content disseminated from the Agency and that certain issues, including transgenic crops, required administrative approval from USDA's Beltsville, MD office before any content could be released. In other words, Kremer noted a significant upscaling of department censorship and "questioning of research", suggesting of the USDA that "the climate now is…we don't want to offend anyone" (https://www.youtube.com/watch?v=UDLdTXe2koo, 24.20). To reiterate the OMB guidelines (discussed above), each agency is given a certain level of latitude, in terms of how research is reviewed and disseminated if it is considered "influential" in relation to private sector interests and public policy (Office of Management and Budget, 2002, p. 8457).

According to an OECD document, it was recognized that patents potentially "hamper further innovation, especially when it limits access to essential knowledge" (https://www.oecd.org/sti/sci-tech/24508541.pdf). In an International Food Policy Research Institute discussion paper, Michiels and Koo (Sept. 2008) also raised a concern regarding the potential constraints that patents create for new knowledge creation and dissemination specifically within public and academic domains. However, Monsanto stated that it endorses an "Academic Research License" (ARL) that "enables academic researchers to do research with commercialized products with as few constraints as

possible. ARLs are in place with all major agriculturally-focused US universities – about 100 in total" (http://www.monsanto.com/newsviews/pages/public-research-agreements.aspx).

In an article discussing confidentiality agreements within the context of academic research, university extension researchers noted that using a company's intellectual property for research allows academic researchers access to ground floor industry materials, technology and resources while providing industry with valuable third party studies and data (http://www.agriculture.com/crops/tech-tour/confidentiality-agreements_196-ar45164). The author also noted that it's a potential symbiotic relationship in theory but in practice, confidentiality agreements, intellectual property rights and patent rights permit industry to limit research parameters and direct research design in a way that may or may not benefit the local needs of university research goals. The author went on to state that it is a system with a built-in imbalance of power in regards to who maintains authority over what and how knowledge is created (ibid).

Michiels and Koo (Sept. 2008) suggested that the U.S. Congress passed the Bayh-Dole Act of 1980 to ensure that not only private parties, but also universities (or other public institution) retain the right to patent or license the results of their research if part of its research project is funded by the federal government. The authors illustrated that from the 1980's to about 2002, privatization in both industry and academics rose significantly in bio-agricultural research as licenses and patents for genetically altered plant processes and traits became incentive to generate, and protect, scientific knowledge (Michiels and Koo, Sept. 2008; http://pazoulay.scripts.mit.edu/docs/generating_ideas.pdf). King and

Hessey (Nov. 1, 2003) noted that in agriculture, the upward trend in biotechnology patents was much steeper than the overall patent. The authors stated that the rise in patents during this period also indicates a marked shift from basic to applied research (ibid). The U.S. government, according to Howard (Oct. 19, 2015) has encouraged private development and ownership rights by 'reduc[ing] the enforcement of antitrust laws and increas[ing] the enforcement of alleged intellectual property infringements' (p.1).

Monsanto and others in the bio-agriculture industry provide statements for the public that state: "Patents encourage and reward innovation" and "patents, for better or worse, may be the only way to provide incentives for innovation while ensuring that a biotech company can recoup development costs" (http://www.monsanto.com/food-inc/pages/seeds-patent-history.aspx; https://www.geneticliteracyproject.org/2014/04/22/patents-and-gmos-should-biotech-companies-turn-innovations-over-to-public-cost-free/). For example, according to Mutz, et al (July 7, 1997) developing the GA21 corn line (glyphosate tolerant pre-cursor to NK603), Monsanto/DEKALB Genetics invested six years and several million dollars. Mutz described that an effective way to try to recoup the financial costs is to shield key techniques and information from its competitors, thus limiting competition from capitalizing on the time and money that Monsanto/DEKALB spent in developing the technology/product (ibid). But, according to Howard, (Oct. 19, 2015) another way to alleviate cost is to consolidate. What used to be an industry populated by small, family-owned businesses is now an industry "dominated by a handful of large, diversified

companies (http://www.nationalacademies.org/includes/genengcrops.pdf). Currently, there are mainly three biotech companies that control "more than half of the global proprietary seed market" (ibid). According to Okoro (May 9, 2005), if one considers the extraordinary number of gene sequence patent applications in just 2002 (~3 million) and the limited number of genes used for agricultural biotechnology, overlapping patents on the same gene has created a complex, costly and time-taking development process that consolidation significantly minimizes. But, McEowen (Sept. 2006) noted that in the case Pullen Seeds and Soils v Monsanto in 2006, Pullen accused Monsanto of monopolizing the glyphosate-tolerant market by "acquiring seed companies that were developing modified seed technology [and] eliminating those projects that could have led to the development of genetically modified seeds that could be used with non-glyphosate herbicide" (ibid).

As stated by Carl Shapiro (2001) "The essence of science is cumulative investigation combined with hypothesis testing. The notion of cumulative innovation, each discovery building on many previous findings, is central to the scientific method" (p. 119). Stanford University's Stanley Cohen and UC-San Francisco biochemist Herbert Boyer were awarded the National Medal for Technology and Innovation for transforming the basic science of molecular biology and the biotechnology industry research and could be argued as initiating the "birth of the biotech industry". Through a "non-exclusive licensing program", developed by Stanford University's Niel Reimer, Columbia University was able to build upon the knowledge of Cohen and Boyer, for a price, and in turn, further advance recombinant DNA techniques to develop DNA transformation,

which Columbia University then patented in the 1980's, http://www.uspto.gov/about/nmti/recipients/1989.jsp; http://www.columbia.edu/cu/21stC/issue-3.1/odza.html; https://www.biotechhistory.org/magazine-article/vital-tools-brief-history-cho-cells/). In an article spotlighting the three Columbia University students who patented DNA transformation (a.k.a. The Axel Patent), the authors noted that these proprietary rights reaped millions in profit for the university as well as the researchers who claimed authorship of the patented discovery, although at the time, according to the article, with two of the three Columbia University researchers on that project (Michael Wigler and Richard Axel), patenting their work was not the motivation for their research. Even after the Columbia researchers patented their discovery, one of the researchers stated that he was still skeptical about its value beyond the university walls. But in the seventeen years that the university owned these patents, it would claim approximately $790 million dollars in private sector licensing fees and that it would become one of the landmark cases for alternative public university revenue (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2750841/#b24). Since the 1980's there has been a significant increase in the number of university patents (in bio-agriculture); but economic success (such that Columbia University experienced) is rare and depends on whether the knowledge or innovation fits a specific commercial need at the right time when it is needed. (Pérez-Peña, Nov. 20, 2013; Dai, Dec. 2007).

Transitions: Basic/Public to Applied/Private Research

According to the United State Department of Agriculture's Economic Research Service (USDA-ERS), investments in public research and development grew most rapidly between 1948 and the 1980's but by 2012, they were six percent lower than 1982, whereas private research and development, since the 1980's, has nearly doubled (http://www.ers.usda.gov/media/1875384/err189_summary.pdf). Paul Berg (Sept. 18, 2008), one of the scientists who organized the Asilomar Conference (see "Perceptions of Safety and Validity" section for more information), posed the question of whether another Asilomar Conference might mitigate the current conflict surrounding the perceived and real risks and benefits of biotechnology between industry, independent and public scientific research, government policy and public perception. Berg suggested several key reasons that such a conference now would not have the productive, transformational impact it did in the 1970's, one of which, in Berg's assessment, is the transition from public to private institutional research which embeds "economic self-interest" as a research priority which, in turn, inhibits researchers from engaging in open, unbiased discussion. According to a 2009 New York Times article, Berg's assessment is echoed by several other scientists (many of whom work for land-grant universities), who voiced frustration at how restricted access to commercial biotechnology outcomes limits the available research on genetically modified crops (Pollack, Feb. 19, 2009). The article detailed that such limitations include: requiring farmers to sign contracts that "prohibit growing the crops for research purposes"; requiring company permission to study its product and often requiring the option for the company to review the study and make

changes prior to publication; and company prerogative to withdraw permission to research after the study was approved and initiated (Pollack, Feb. 19, 2009).

A group of 26 scientists, hired by the USDA and EPA as part of a Technical Advisory Committee for "Regional Research Projects NCCC-46 'Development, Optimization, and Delivery of Management Strategies for Corn Rootworms and Other Below-ground Insect Pests of Maize'" submitted the following formal statement to the EPA in 2008, but according to Don Huber (personal communication, June 9, 2016), the 26 scientists would not sign their name to the statement because to do so could have resulted in them losing their jobs.:

> Technology/stewardship agreements required for the purchase of genetically modified seed explicitly prohibit research. These agreements inhibit public scientists from pursuing their mandated role on behalf of the public good unless the research is approved by industry. As a result of restricted access, no truly independent research can be legally conducted on many critical questions regarding the technology, its performance, its management implications, IRM, and its interactions with insect biology. Consequently, data flowing to an EPA Scientific Advisory Panel from the public sector is unduly limited. (See Appendix 7)

The experiences of the above referenced scientists, along with the barriers described in Berg's assessment, contrast with Ury's (1993) suggestion that "[y]ou get the most satisfying solutions and the most optimal relationships when both sides are doing their best to engage the very real problems dividing them" (p. xi).

Unpublished Data

The scientists referenced above expressed frustration with how patent rights and confidentiality agreements limited the researchers' capacity to not only explore beyond the scope and focus of industry interests but also to obtain permission to research patented products in the first place. Evidence of limited public and independent research is evidenced in how research is represented in glyphosate and NK603 applications, assessments and approvals. For example, glyphosate was assessed and re-registered by the EPA, in 1993, citing over 100 non-published industry studies (the majority of which were from Monsanto) in its reference sections to support the assessment criteria (EPA, Sept. 1993). The International Program on Chemical Safety (INCHEM), a collaboration between the U.N., the WHO and the International Labor Organization, published a review of glyphosate in 1994 in which approximately 150 of the 350 studies listed in the reference section were unpublished studies, the majority of which were submitted by Monsanto (http://www.inchem.org/documents/ehc/ehc/ehc159.htm). The FAO has also been an active partner with EFSA and WHO in evaluating glyphosate. In seeking data from governing sources, I found a Google Book preview of the UN's Food and Agriculture Organization's 2005 publication regarding pesticide residues in food, which showed the References listed for glyphosate and of the approximate 112 studies referenced by the FAO for glyphosate, over 100 were unpublished studies conducted by researchers from (listed in order of majority contribution) Monsanto, Cheminova (a Danish pesticide maker), Zeneca (a biopharmaceutical company) and Syngenta (https://books.google.com/books?id=yIlSy6UZJjwC&pg=PA474&dq=Food+and+Agricu

lture+Organization+2005+pesticide+residues+glyphosate&hl=en&sa=X&ved=0ahUKEwj3_aWa_-bPAhXG4iYKHU2SCCMQ6AEINjAA#v=onepage&q=Food%20and%20Agriculture%20Organization%202005%20pesticide%20residues%20glyphosate&f=false). In an FAO/WHO (2016) international glyphosate assessment it was stated that "[t]he current meeting evaluated all previously considered toxicological data in addition to new published or unpublished toxicological studies and published epidemiological studies on cancer outcomes…[and] [t]he evaluation", but the references were not listed according to study (p. 19).

According to Portier's et al (Mar. 3, 2016) comparative analysis between IARC's and the EFSA's glyphosate assessments, the EFSA's (2015) report, illustrates that the evidence considered in policy-making is still weighted in favor of industry. Portier and a group of ninety-three other scientists (microbiologists, biomedical cancer researchers, biochemists, molecular and cellular biologists, pathologists, epidemiologists, etc.) co-authored an article (which was first submitted as a letter to EU's Commissioner Health & Food Safety, Vytenis Andriukaitis on Nov.27, 2015) comparing the WHO IARC and the EFSA glyphosate assessments. They analyzed the studies used in the assessment as well as how the assessment was conducted. Their conclusion emphasized that the BfR assessment lacked credibility because it relied on non-published industry research that were not accessible to the public, suggesting a significant lack of transparency (Portier, et al Mar. 3, 2016).

General Barriers

Unpublished industry studies were not the only challenge to researching data on Roundup, inert ingredients, NK603 and other transgenic crops. For example, trying to find information on polyethoxylated tallowamines (POEAs) on the EPA's website has been challenging. After trying various key words (e.g. polyethoxylated tallow amines; tallow amines; tallowamines; tallow; polyethoxylated; POEA, etc.) in the main website, NCEP and archives, my search produced only an extremely limited description for Tallowamines as a pre-harvest application covered under §180.920 which exempts it from tolerance requirements, describing it as a surfactant or adjuvant: "Tallowamine, ethoxylated, mixture of dihydrogen phosphate and monohydrogen phosphate esters and the corresponding ammonium, calcium, potassium, and sodium salts of the phosphate esters, where the poly(oxyethylene) content averages 2-20 moles (CAS Reg. No. 68308-48-5)" and does not exceed 20% of the formulation https://iaspub.epa.gov/apex/pesticides/f?p=INERTFINDER:3:::NO::P3_ID:6832. According to the information listed on the EPA's Substance Registry Services, the main distinction between CAS number 68308-485 and CAS number 61791-26-2 appears to be that the former includes phosphates but does not provide a product name (e.g. MON 0818—see below). A search using the EPA CAS number 61791-26-2, which was listed in the above EPA Federal Register notice (Jul. 7, 1995), provided a little more detail that described the inert pesticide ingredient, POEA, as "Tallow alkyl amines ethoxylated" but the substance was categorized as List 3 (unknown toxicity). The information provided is extremely limited and does not provide any details about how the substance was assessed

(EPA, Sept. 15, 2015). Noting that the technical name for POEA (that the EPA used in a memo assessing two Roundup product labeling requirements—see "Data gaps" for more information), polyoxyethylene alkylamine, differs from the term, polyethoxylated tallowamine (which is used in a multitude of other sources), I searched the EPA's National Service Center for Environmental Publications (NSCEP) using the EPA's term and CAS number. One of the four search results was a 1992 "List of Pesticide Product Inert Ingredients"; inserting the CAS number into the NSEP search box for this document resulted in one "hit", which did not have a CAS number next to it but was described as "Soap (Source undefined)". The document stated that "OPP records do not readily permit the confirmation of the presence of any given listed inert in currently registered pesticide products" (https://nepis.epa.gov/Exe/tiff2png.cgi/9101W9JG.PNG?-r+75+-g+7+D%3A%5CZYFILES%5CINDEX%20DATA%5C91THRU94%5CTIFF%5C00002966%5C9101W9JG.TIF). One of the remaining three search results was the EPA's Substance Registry Services, which provided a list of statutes, regulations and EPA applications/systems and valid synonyms, including Mon 0818, which presumably, is the product name linked to the CAS number. However, neither of the CAS numbers listed above shows the common name "polyethoxylated tallowamine" in its "synonym" list (https://ofmpub.epa.gov/sor_internet/registry/substreg/searchandretrieve/substancesearch/search.do?details=displayDetails&selectedSubstanceId=15792#HealthAndOther). In terms of searching for particular glyphosate studies, several studies are referenced as supporting evidence for the EPA Tier One Endocrine Screening Assays for glyphosate conclusions (e.g. MRID 4886510 and 48671305), but those studies cannot be found

anywhere else on EPA's current, archive and National Service Center for Environmental Publications (nepis.epa.gov) websites.

In regards to transparency in the current conflict about glyphosate, obtaining an online version of the recent glyphosate assessment that Germany was tasked to conduct—the BfR report—is proving extraordinarily difficult to find, in its full and original report, as is obtaining the draft report that BfR submitted to EFSA that summarized this study, thus limiting my access to the basic design and timeline of the study. Multiple key word/phrase searches (e.g. BfR; BfR report; German Rapporteur Member State glyphosate; glyphosate assessment; RMS glyphosate; etc.) in various search engines and within the EFSA website show no results for the BfR report. Several internal links within the EFSA website where related information should have been available result in pages displaying: Server Not Found. In addition, along with the EFSA public statement regarding their conclusions about the peer review of BfR's draft as an assessment response to IARC's "probable carcinogen" claim, the EFSA includes a link to the WHO's IARC report but when clicked, displays the message: The Page You Have Requested Does Not Exist (http://www.efsa.europa.eu/en/press/news/150730). Portier, et al (Mar. 3, 2016) noted that the BfR evaluators were not listed and the studies used in their assessment were unpublished and not publicly accessible. The EFSA continued, stating that they disagreed with Portier et al's (Mar.3, 2016) conclusion that BfR's assessment process was not transparent and that all of the "related background documents which run to around 6,000 pages have been published on EFSA's website" http://www.efsa.europa.eu/en/press/news/151119a (ibid, p. 2). Accessing the documents

for glyphosate from this website, however, requires one to submit their personal information in an online document request form. In my web search (described above) this page did not appear. Stated on the homepage of this website, however, the EFSA claims that the BfR report is accessible, but in "updated" form "to take account of comments and discussions during the peer review…" (http://www.efsa.europa.eu/en/press/news/151119a). In other words, the original assessment report is not available.

Theme 3: Data Gaps

Roundup received its first pending registration with the EPA in 1974 and was subsequently marketed as a broad spectrum herbicide. Although the original registration for Roundup and/or glyphosate seems to be absent from the EPA's National Service Center for Environmental Publications (NSCEP) document database, a simple search for pre-1976 information on glyphosate produces eight results, one of which discussed tolerance levels and indicated that by 1975 several glyphosate tolerance levels were established but there were no toxicology studies referenced to support why or how those levels were determined. In that document, the EPA stated that glyphosate toxicity was minimal but admitted that the mode of action for glyphosate was "not know[n]; may inhibit the aromatic amino biosynthesis" (Office of Pesticides Program, Mar. 30, 1977; EPA, 1975, www.gao.gov.assets/120/11 p.ii). Within a few years after Roundup was registered, it was noted that "while there are ample toxicity studies at hand concerning this material, there is no information available concerning the mechanism whereby the compound affects mammalian systems", including how it is metabolized (Bailey, n.d.).

By 1975, according to a GAO report, there were 35,000 pesticides (new and existing) in the U.S. that needed to be evaluated according to current scientific standards. Many pesticide tolerance levels were outdated and many (approximately 140 out of 230 active ingredients) were not even tested (GAO, Dec. 4, 1975). The GAO (ibid) report of the EPA also indicated several factors contributing to the Agency's failing to meet these goals, emphasizing that in regards to protecting public health and the environment, the GAO stated that for several pesticides, the EPA failed to obtain appropriate studies to assess many of the pesticides' short and long-term impact on reproductive health, child growth, and genetic changes (ibid). According to a later report, the EPA expressed frustration at how difficult it was to obtain appropriate studies from registrants in a timely manner (Eschwege, Aug. 7, 1980). Similarly, the EFSA noted several data gaps and inconsistencies between applicant (glyphosate manufacturers) claims and their supporting evidence (Monsanto included) (EFSA, 2015). In addition, in 2013, the GAO noted that

> [t]he extent to which EPA ensures that companies submit additional required data and EPA reviews these data is unknown. Specifically, EPA does not have a reliable system, such as an automated data system, to track key information related to conditional registrations, including whether companies have submitted additional data within required time frames. (http://www.gao.gov/products/GAO-13-145)

By the 1980's, according to a GAO (1986) report, the EPA still needed to revise their assessment system as the number of new applicants for registration continued to stack on top of a growing backlog of existing ones and the EPA was unable to keep up.

By the mid-1980's, there were 50,000 pesticides with 600 different active ingredients and 900 different inert ingredients (ibid). The GAO (1986) review also noted that the EPA had only been able to complete approximately 124 preliminary assessments of active ingredients—in approximately 15 years. In addition, the GAO (ibid) review emphasized concerns regarding the lack of substantive subchronic and chronic toxicity assessments. (Interestingly, that was the same year that glyphosate was being reviewed for reregistration—as discussed in the "Perceptions of Safety and Validity" section). I searched ProQuest's Biological Sciences database using the search terms "tox*" AND "glyphosate*" OR "Roundup" in the abstract for peer reviewed toxicological studies on glyphosate/Roundup prior to 1994; but the majority of the studies, 26 out of 30 results, focused on how the pesticide (mainly the active ingredient glyphosate) functioned as an herbicide on various crops, aquatic life and insects but there were only four (publicly accessible) toxicological studies that tested the impact of glyphosate and/or Roundup on mammals and/or or humans. Three of the four studies analyzed the toxic impact (on human health) of the surfactant used in Roundup formulations (POEA) and one analyzed the toxicity of glyphosate on an Australian bird, rodent and marsupial species. According to the abstracts, the overall conclusion from these four studies indicated that glyphosate was mildly toxic but the Roundup formulation and surfactant (POEA) was much more toxic (ibid). However, as the numbers indicate, the studies are limited. Tomerlin (May 8, 2006), noted that by 2006, the EPA also "lack[ed] sufficient monitoring exposure data to complete a comprehensive dietary exposure analysis and risk assessment for glyphosate in drinking water. Likewise, in the E.U. the EFSA's (2015) report also stated that there

are multiple gaps in the research in such areas as pesticide residue levels and water toxicity.

In the most recent re-registration of glyphosate, the EPA noted that it was "seeking toxicity data on formulated products containing the surfactant POEA, due to uncertainty about its risk to aquatic animals" (but in the assessment report, there was no mention in the requirement about POEA toxicity tests in regards to human health) (EPA, June 17, 2009). However, in a 2010 memo, the EPA stated that "[i]t is known from toxicity testing in the open literature that one surfactant mixture that has been used in glyphosate products is considerably more toxic to aquatic organisms than technical glyphosate. That surfactant is polyoxyethylene alkylamine mixture (POEA, CAS number 61791-26-2)", however, there are "no studies…available for POEA alone" (https://www3.epa.gov/pesticides/chem_search/cleared_reviews/csr_PC-103613_26-Oct-10_a.pdf). (See the "Data Access Restrictions: General barriers" section for more information on CAS number 61791-26-2).

In terms of beginning to fill prior data gaps, according to the article abstracts discussed above (found in ProQuest's Biological Sciences database using the search terms "tox*" AND "glyphosate*" OR "Roundup" in the abstract for peer reviewed toxicological studies on glyphosate/Roundup prior to 1994), some of the studies indicated evidence that the mode of action of glyphosate was beginning to be understood by the mid to late 1980's and by 1991, had been determined. Several of the other studies in the results list discussed the microbiological impact that glyphosate had on crop root systems. According to the abstracts for those articles, the outcomes were mixed,

depending upon which study was referenced, between indicating that the presence of glyphosate promoted hazardous or non-hazardous pathogenic microbial growth (ibid). A 1982 OECD report stated that “it would be extremely short–sighted to neglect studies of microbial taxonomy and descriptive ecology: the bottle–neck which can arise here is the lack of awareness by the applied scientist and technologist of the richness of microbial types and activities” (Bull, Holt and Lilly, 1982, p. 23). The 1982 OECD report also noted that “strong support will be necessary to increase basic knowledge of plant physiology and plant genetics if governments want the expected agricultural impacts of biotechnology to materialize” (ibid, p. 10). Bull, Holt and Lilly (1982) also noted that although microbiology was considered, at the time, more advanced than plant science, microbial physiology was “almost a universal bottleneck” where “[i]ndustry does little or no fundamental research in this discipline which thus needs public support” (p. 10). Recently, government and academic researchers such as Dr. Huber (plant pathologist), Dr. Kremer and Dr. Lucero (microbiologists) have expressed that the U.S. federal recognition, time and resources that are needed to appropriately conduct safety studies on GMO’s, as well as the impact that glyphosate and other agricultural chemical inputs have in the environment and on public health, is sorely inadequate (https://www.youtube.com/watch?v=UDLdTXe2koo). The National Academies of Science, in 2004, stated that ‘‘there remain sizable gaps in our ability to identify compositional changes that result from genetic modification of organisms intended for food’’ (NAS, 2004, p 15). A recent National Academies of Sciences, Engineering and Medicine report (2016) stated that “[m]olecular biology has advanced substantially since

introduction of GE crops two decades ago" and should be further invested in as a strategy to "address food security and other challenges", emphasizing that omics technologies need further development to effectively test for and analyze unintended effects from GE and conventional "new crop varieties" (ibid, p. xviii). However, the report concluded that the current scientific data does not offer conclusive evidence that consumption of genetically engineered crops is hazardous to human health.

One method that the U.S. has utilized to help limit exposure to health hazards is the USDA and FDA pesticide residue assessment programs. Since its implementation in 1991, the EPA had been using the USDA's Pesticide Data Program (PDP) results to help determine dietary exposure levels of pesticides during its RED (Reregistration Eligibility Review) reviews for existing pesticides. The EPA provides the USDA with a list of pesticides to assess based on "compounds with acute and chronic endpoints, including suspected carcinogens," however, since the implementation of the program in 1991, glyphosate has not been included (USDA, April 1994). A recent GAO (Oct. 7, 2014) report recommended that the USDA and FDA revise their pesticide residue programs to better reflect consumer exposure. But the USDA does not choose which pesticides to test; instead, that decision comes from the EPA's recommendations. The EPA reasoned that glyphosate was demonstrated to be a low-level hazard concern and thus did not warrant costly assessment. Echoing this response, the FDA and the USDA added that glyphosate residue tests were more cost prohibitive compared to other pesticides and, therefore, rarely tested (Davies, Feb. 17, 2016; Gillam, Apr. 20, 2015). The FDA and a GAO (Oct. 2014) report further explain that the FDA has not included glyphosate in its annual

monitoring studies mainly because it requires costly "selective residue testing" (GAO, Oct. 2014, p. 7; FDA, 2012; FDA, 2006). In addition, the GAO (Oct. 2014) report stated that the FDA "does not disclose the pesticides with tolerances for which it does not test or the potential effect that not testing could have on its detection of violations" (p. 55). The FDA responded to these concerns suggesting that it was weighing the cost of implementing glyphosate testing methods with the "extent of the use of genetically engineered crops for human foods" (GAO, Oct. 2014, p. 26). Since the USDA began its Pesticide Data Program in 1991 to the most recent sampling results of 2014, according to the yearly USDA PDP datasheets, sweet corn (canned or frozen) was often tested, but corn as a grain was only tested in 2007 and 2008 and glyphosate residue was apparently only tested once, on soy, in 2011 (https://www.ams.usda.gov/datasets/pdp/pdpdata). The GAO (Oct. 2014) report also suggested that the FDA work with the OMB in developing a comprehensive list of pesticides (that have pesticide residue levels) that have and have not been tested. The GAO report also suggested that the FDA develop a more public-friendly means of disseminating this information in order to decrease the potential for misinformation (ibid).

Theme 4: Perceptions of Safety and Validity

Introduction

In a 1976 Congressional hearing, agricultural biotechnology was introduced as a potentially safer (and more lucrative) method than conventional agriculture, but being a new field of study using new technologies, there were also great reservations regarding its safety. Participants in the hearing discussed the need for appropriate research in order

to determine the parameters of safety, viability and applicability of this new science and technology (94th Congress, May 11, 1976). Berg (Sept. 18, 2008) stated that by the 1970's, the promise and potential of biotechnology could be envisioned not only for the medical and pharmaceutical field, but for agriculture as well. However, Berg continued, there were mixed messages from the innovators—researchers/scientists—as initial excitement and promising potential of a new and exciting field of research was tempered with scientists calling for a moratorium on r-DNA work until a more thorough risk assessment was performed (Berg, Sept. 18, 2008).

The Asilomar Conference was a group of 140 scientists, government representatives, journalists and lawyers who, in 1973, met in California to discuss the risks and merits of r-DNA research. Throughout the conference quite "often scientists willingly acknowledged the risks in other's experiments but not in their own" (Berg, Sept. 18, 2008, p.290). However, after much debate, the Asilomar conference participants were able to reach a consensus for a set of risk management strategies that satisfied everyone and set the stage for future r-DNA research and regulatory guidelines (Berg, Sept. 18, 2008).

The OECD worked collaboratively with member nations and relevant stakeholders, including industry and organizational interests, to develop a multitude of toxicology testing guidelines that would make international trade safer, for the public and environment, and easier for commercial interests (FDA, Mar. 1, 1994). According to an OECD report (1986), the safety of biotechnology was established, based upon three "compelling lines of evidence": 1.) risk assessment studies had "failed to demonstrate"

that transferred DNA could create “unexpected hazardous properties” in the host organism, 2.) “more rigorous evaluation of existing information regarding basic immunology, pathogenicity and infectious disease processes has resulted in the relaxation of containment specifications recommended by national authorities”, and 3.) “the experimentation conducted in recent years has elicited no observable novel hazard (p.27).

Transitions: Basic to Applied Research

Cramo, Brewer and Lac (2015) discussed the limitations of applied research/R&D, stating: “To the extent that applied research is restricted to the examination of variations in a particular A-B relationship, it is unlikely to uncover an explanatory principle that accounts for C-D and E-F, *along with* A-B” (Cramo, Brewer and Lac, 2015, p. 31). In other words, the authors suggested that applied research/R&D are extremely useful tools to use when there is a specific need to fill but innovative processes or products are not arrived at or sustained in a bubble. To ensure public and environmental safety this research must also be open to criticism and change that includes holistic exploration surrounding the impact (potential and real) of implementing the new process/product (ibid). However, in a public meeting addressing the FDA’s 1992 policy for regulating bioengineered crops, it was stated: “It is the characteristics of the organism, the environment and the application that determine risk or lack thereof, of the introduction not the technique used to produce the organism” (FDA, Oct. 30, 2015).

By 1992, there were approximately 30 different genetically engineered crops being field tested in the U.S. According to the FDA, the benefits of utilizing genetic engineering would provide safer, more consistent and desirable outcomes than, for

example, the less precise and less reliable mutagenic techniques or the more times-taking gene transfer techniques (FDA, Oct. 30, 2015). According to the FDA, bio-agricultural technology was considered an improvement to the traditional agricultural system. But the FDA reiterated that this did not suggest that the U.S.'s traditional crop development was unsafe, but that it is because of the U.S.'s long history of safe traditional crop development that the FDA derived confidence in considering bio-agricultural technology as simply another step in improving agricultural systems (ibid).

But how does one arrive at a determination of "safe"? A survey of sixty-two life sciences researchers suggests that funding sources and professional training influence individual perceptions regarding the safety and predictability of transgenic crops. The survey found that:

> Scientists with industry funding and/or those trained in molecular biology were very likely to have a positive attitude to GM crops and to hold that they do not represent any unique risks, while publicly-funded scientists working independently of GM crop developer companies and/or those trained in ecology were more likely to hold a "moderately negative" attitude to GM crop safety and to emphasize the uncertainty and ignorance involved. (ENSSER, Oct. 21, 2013)?

Kahan, et al's (2013) study explains how one's culture influences how individuals interpret scientific or mathematical information, concluding that professional affiliations influenced one's perception of scientific or mathematical interpretations. Another study analyzed 94 peer reviewed articles "that report on health risks or nutritional value of genetically modified food products" and concluded that there was "a strong

association…between author affiliation to industry (professional conflict of interest)" and "study outcomes that cast genetically modified products in a favorable light" (Diels, et al, 2011).

In a recent New York Times article the authors described how academic researchers are being selected and supported by private funders to speak on behalf of industry interests in an effort to improve stakeholder, policy makers and public credibility (http://www.nytimes.com/2015/09/06/us/food-industry-enlisted-academics-in-gmo-lobbying-war-emails-show.html?_r=0). Although the article focuses on a specific academic researcher who was hired by Monsanto to promote agricultural biotech crops, it points out that academic researchers are also working for the organic food industry. The New York Times collected and reviewed several documents and emails communications from the academics who worked for the organic industry and concluded that while [t]here was no evidence that academic work was compromised" the emails did illustrate a trend from academics to lobbying for both organic and agricultural biotechnology interests. According to the article, the emails they evaluated from academics who worked for the agricultural biotechnology industry

> provide a rare view into the strategy and tactics of a lobbying campaign that has transformed ivory tower elites into powerful players. The use by both sides of third-party scientists, and their supposedly unbiased research, helps explain why the American public is often confused as it processes the conflicting information. (ibid).

The article quoted an agricultural biotechnology company email response to a researcher whom they had recently hired which stated that hiring academic researchers was “a new way to build trust, dialogue and support for biotech in agriculture” (ibid).

Weight of Evidence

In the 1960’s, claims of safety for the PCB industry (e.g. Bayer, Monsanto, Brush Wellman, Exxon), according to Le Menestrel and Rone (2013), were based on a lack of certainty that their product caused harm (i.e. operating from the perspective of scientific uncertainty in which industry claimed that additional research was needed to conclusively verify hazard). LeMenestrel and Rone (2013) stated that contrary to those previous industries, whose products were removed or limited from the market due to lack of convincing evidence of safety, agricultural biotechnology companies have produced, in conjunction with academic and industry-supportive researchers, an extensive amount of data from which to make scientifically-backed claims of safety. However, an OECD (Apr. 13, 2012) Guidance Document stated that “[a] reasoned scientific approach to the assessment of substances for chronic toxicity or carcinogenicity must first include an assessment of all available information that has the potential to influence the study design” (p. 25).

A search on the EPA’s archive website produced a multitude of internal memos containing registration and toxicological data (mainly derived from or in regards to industry data) for glyphosate and various formulations of Roundup and other pesticides (https://archive.epa.gov/pesticides/chemicals/foia/web/pdf/103601/103601.htm).

The EFSA's (2015) glyphosate assessment contrasts with that of the IARC, concluding that the active substance glyphosate is "unlikely to pose a carcinogenic hazard to humans" (p. 1). The EFSA (2015) stated that "[in reference] to the unusually large data base available, it was considered appropriate by the EU Expert peer review to adopt consistently a weight of evidence approach" (EFSA, 2015). According to Balls, et al (Dec. 2006), using a "weight of evidence approach" is usually considered in situations of uncertainty. However, Balls, et al (ibid) analyzed 272 studies, concluding that in approximately one third of those studies, there was "frequent lack of definition of the term, multiple uses of the term and a lack of consensus about its meaning, and…many different kinds of weights, both qualitative and quantitative" (Balls, et al, Dec. 2006). An OECD (Apr. 13, 2012) Draft Guidance Document on the Design and Conduct of Chronic Toxicity and Carcinogenicity Studies stated that the "weight-of-evidence approaches differ among OECD countries and regulatory sectors" (p. 26).

Parts vs Whole: CP4 enzyme and NK603

According to OECD (1986; 1992) reports, the microbiology and plant pathology research needs mainly focused on the potential problem and solution for super-weeds and superbugs. Data and discussion in the 1986 OECD report emphasized microbial research for its potential contributions to reducing pesticides through r-DNA techniques and development. Of concern, according to the report, was the possibility that micro-organisms from trans-genetic processes might create, host or alter pathogens that might cause plant and/or human disease. However, the 1986 OECD report reasoned that "[s]ingle gene modifications of micro-organisms with no pathogenic potential or history,

or introduction of several genes contributing to pathogenicity, do not appear likely to result in unanticipated pathogenicity" (p.29). Subsequent risk assessment was developed, according to the 1986 and 1992 OECD reports, on the premise that the r-DNA technique was accurate, predictable and safe, posing no more risk to human or target plant health than conventionally grown plants (OECD, 1986; OECD 1992).

An OECD (1993) follow-up to their 1986 guiding principles report discusses the merits of substantial equivalence, reasoning that just because a food is genetically altered does not make it inherently unsafe. By 1996, an overview of biotechnology by the OECD stated that "[t]he great controversies over DNA recombination *per se* are more a thing of the past than of the future" (Wald, p. 9). But later Wald (1996) comments about how biologists have been persistently "overly-cautious" about the rate and state of agricultural biotechnology (p. 16). The controversies that had largely been resolved, according to the 1996 OECD report, encompassed an array of uncertainties regarding potential health and environmental hazards but even by the mid-1980's, when the U.S., as well as the OECD, was debating about the risk and benefit of agricultural biotechnology, the discussions focused mainly on environmental risk (because existing toxicological studies and how their results were interpreted allayed fears regarding at least immediate foreseeable health risks) (Sheingate, Apr. 2006).

The health risks that had been of particular concern with NK603 was the plant pathogen used to develop the CP4 enzyme that enables the plant to withstand glyphosate. The OSTP (June 26, 1986) however, had set the tone early on stating that "[i]t should be noted that microorganisms play many essential and varied roles in agriculture and the

environment …and as a rule these agricultural and environmental introductions have taken place without harm to the environment" (p.5). In 1992, the FDA (reiterating its role in determining how GE crops are assessed and regulated) interpreted the Federal Food, Drug and Cosmetic Act to include bio-engineered food regulation in the same category as traditional food. According to the FDA:

> The regulatory status of a food, irrespective of the method by which it is developed, is dependent upon objective characteristics of the food and the intended use of the food (or its components). The method by which food is produced or developed may in some cases help to understand the safety or nutritional characteristics of the finished food. However, the key factors in reviewing safety concerns should be the characteristics of the food product, rather than the fact that the new methods are used. (FDA, May 29, 1992).

Per FDA policy, if the genetically modified product is "generally recognized as safe" (GRAS) or if it can be proven to be substantially equivalent to its conventional counterpart, it does not have to undergo federal regulation (http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm). Consequently, in 1993, the OECD guidelines adopted this policy as well (https://stats.oecd.org/glossary/detail.asp?ID=2604).

USDA reported that field trials for NK603 demonstrated that "there were no deleterious effects on plant, non-target organisms, or the environment" (APHIS, Aug. 30, 2000). However, it should be noted that when APHIS simplified GMO registration procedures (discussed above), they also simplified GMO field testing by "reducing the

field test reporting requirements for certain multi-year field trials" (APHIS, Apr. 24, 1997). But Monsanto reasoned that, like GA21, NK603 was not a plant pest (e.g. it was not found growing wild and they claimed that pollination drift to other fields could be managed; it would not damage commodities or harm non-target or beneficial species) and APHIS granted it non-regulated status, which means it can be grown and transported within the U.S. without federal oversight (APHIS, Aug. 30, 2000).

"Section 402(a)(1) of the [Federal Food, Drug and Cosmetic] act is most frequently used by FDA to regulate the presence in food of unavoidable environmental contaminants such as lead, mercury, dioxin, and aflatoxin" (FDA, May 29, 1992). The FDA's main obligation in food safety is post-market but if (in the case of genetically engineered components) the genetic component is thought to be a potential health concern then the FDA would initiate a pre-market investigation (FDA, May 29, 1992). However, because of the historically safe development of traditional plant breeding techniques, "the FDA has not found it necessary to conduct, prior to marketing, routine safety reviews of whole foods derived from plants", including plants derived from biotechnology (FDA, May 29, 1992). According to a cross-agency report titled "Agricultural Biotechnology Risk Analysis Research in the Federal Government", toxicology and allergenicity research and assessments focus only on the individual protein that is inserted into the plant DNA (AGRA, 2004). If the protein inserted into the plant DNA is considered toxicologically safe it is assumed that the subsequent plant will not pose a risk any different than its conventional counterpart. When Monsanto submitted their petition to the USDA's APHIS for non-regulated status for NK603, they concluded

stating that "NK603 was demonstrated to be equivalent to both the E. coli-expressed CP4 EPSPS protein used for safety studies and CP4 EPSPS expressed by a commercial RR soybean variety" (Croon, Jan. 7, 2000). Now for a little layman's science…the EPSPS enzyme is in all plants as part of the shikimate pathway, which helps plants biosynthesize aromatic amino acids, which are critical for plant survival. Glyphosate tolerant plants, however, have an altered EPSPS enzyme called CP4 (which is derived from agrobacterium and cauliflower mosaic virus) EPSPS that enables the plant to tolerate glyphosate. Glyphosate binds to the CP4 EPSPS enzyme in a way that, according to some, does not inhibit the growth of an herbicide (glyphosate) tolerant plant (Funke, July 12, 2006).

In terms of human consumption of transgenic herbicide tolerant plants Monsanto presented the results of an acute oral toxicity mouse study, which was submitted in support of Monsanto's initial transgenic crop registration petition. Monsanto concluded that CP4 EPSPS is as safe as a plant's natural EPSPs, explaining that the mice were given the purified CP4 EPSPS protein at rates much higher than normal consumption would be expected before a NOEL was reached (https://www.aphis.usda.gov/brs/aphisdocs/00_01101p.pdf; https://www.aphis.usda.gov/brs/aphisdocs/93_25801p.pdf). "Acute" studies, according to OECD standards, are typically high dose studies conducted on 6-9 animals for a period of less than twenty-eight days (OECDa, Sept. 21, 1998).

Monsanto also presented the results of feeding studies using conventional soybeans and the glyphosate tolerant soybeans on rats, cows, chickens, catfish and quail

that ranged from 5 days to 10 weeks. Monsanto concluded from these tests that "All…samples tested provided similar growth and feed efficiency for rats, chickens, catfish and quail. The nutritional value or wholesomeness of GTS [glyphosate tolerant soybeans] 40-3-2…was the same as conventional varieties of soybeans" (Results of the cow test were not mentioned.) (http://cera-gmc.org/GmCropDatabaseEvent/GTS%2040-3-2). Based on the studies presented in the GTS 40-3-2 petition for non-regulated status, Monsanto petitioned for NK603, highlighting the similar technology and attributes between the two illustrates that NK603 is as safe as GA21, which was illustrated to be as safe as GTS 40-3-2 and thus merits similar judgment regarding regulatory status. The data used to evaluate the safety of the CP4 EPSPS enzyme and NK603 as a whole was provided by Monsanto. In response to Monsanto's petition for non-regulated status for NK603, the FDA stated:

> Monsanto has concluded that its transgenic NK603 corn is not materially different in terms of food safety and nutritional profile from non-transgenic corn hybrids currently on the market. At this time, based on Monsanto's description of its data and analysis, the agency considers Monsanto's consultation on the Roundup Ready® NK603 corn line to be complete. (FDA, Oct. 9, 2000).

The European Commission clarifies, however, in (EC) Regulation 1829/2003 that "[w]hilst substantial equivalence is a key step in the procedure for assessment of the safety of genetically modified foods, it is not a safety assessment in itself" (EC, Sept. 22, 2003, no. 6). The Regulation also includes a recommendation that "genetically modified

food and feed should undergo a safety assessment through a Community procedure before being placed on the market" (E.C., Sept. 22, 2003, no. 3).

From 1994 to 2000 (when NK603 was introduced to the EU's Spanish Competent Authority), the EU had received twenty-four petitions for various crops (e.g. potatoes, cotton, corn, rapeseed, sugar beets, tomatoes and soybeans), the majority of which were submitted by either Syngenta, Bayer or Monsanto. Currently, however, there are a multitude of transgenic crops that have been approved for importation but only one, Mon 810 (Monsanto's Bt corn, in which the Bt toxin is inserted in the plant genes to protect against the European corn borer) has been approved for cultivation—the majority of which is grown in Spain (http://www.isaaa.org/). When the Spanish Competent Authority (CA) assessed and approved NK603, the application and materials were then submitted to the EFSA for further evaluation concluding that?

> according to the current state of scientific knowledge and after examining the existing information and data provided by the Monsanto Company, the Spanish Commission on Biosafety could give a favourable opinion to the commercialisation in the E.U. of maize NK603 if proposals and conditions established in the ERA report are implemented. (EFSA, May 27, 2009)

The original application for NK603 included a request to approve it for food, feed and cultivation, but the application was later modified, retracting the request for cultivation approval (only one transgenic crop – Bt Corn – is cultivated in the E.U.). As part of required materials for E.U. approval for importing NK603, Monsanto submitted the Acute study (discussed above) in which mice were given oral doses of the CP4

EPSPS enzyme, although the EFSA emphasized that it did not advocate these tests since the naturally occurring protein was not found to be a health risk. Monsanto also submitted sub-chronic toxicity studies which indicated changes in the blood in the high dose female rat group. The panel agreed with Monsanto's conclusion that because "no other observations of treatment related effects were made" the variations did not indicate statistical or significant biological findings (EFSA, 2003, p. 9). Monsanto also conducted a supplemental "13 week safety assurance study" for NK603 in which ten groups of rats with twenty rats per sex per group were tested (Hammond, Dudek, Lemen and Nemeth, Feb. 12, 2004). The minimum requirement for subchronic toxicity studies (i.e. 90-day studies) 10 rats/sex/group according to OECD standards (OECDb, Sept. 21, 1998). However, the blood and urine analysis was conducted on ten out of the 20 rats per sex per group, the results of which, as stated by Monsanto, did not produce statistically significant differences. In Monsanto's report describing this study, there is no explanation regarding the other half of the test subjects (ibid).

By 2004, the EC approved, by default (i.e. E.U. Committee and Council members did not reach a majority vote so the E.C., according to legislative rules, approved it), NK603 for food and feed purposes (E.C., July 19, 2004). Of the approximate 131 GMO varieties that were brought to the Commission for decision, from 2004-2015, sixty-six of them resulted in Council votes that did not reach majority consensus, which means that approximately half of the GMO products, in the E.U. market, were approved by default rather than majority consensus (http://ec.europa.eu/food/dyna/gm_register/index_en.cfm). In the case of NK603, there were twenty-five member states voting, nine voted in favor,

nine voted against and seven abstained. In looking at the individual votes, there were 124 total votes, forty-eight voted in favor, forty-three voted against and thirty-three abstained. A qualified majority for 124 votes is sixty-two. Just recently NK603 registration was up for renewal and it was granted by default, again, as neither the Standing Committee nor the Council rejected the renewal or was able to reach a qualified majority vote (EC, Apr. 4, 2015; http://europa.eu/rapid/press-release_IP-15-4843_en.htm).

Parts vs Whole: Glyphosate, Inerts, Roundup

The Office of Strategic Development (Nov. 1995) emphasized the need for the EPA to develop an assessment system to achieve a more integrated approach to the human ecology. The EPA developed criteria for a multitude of studies that, for example, address the chemical impact on wildlife (birds, mammals and aquatic), plant life, water quality, soil quality, reproduction, worker safety, carcinogenicity, etc. However, by 1997, the EPA stated that it did not know how to identify and integrate common mechanisms of toxicity with cumulative exposure and risk assessments, but it was assumed that glyphosate did not pose a danger because it "[did] not appear to produce a toxic metabolite produced by other substances". The EPA stated that future reregistration, however, would require the registrant to provide common mechanism of toxicity data. (https://www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/tred_PC-417300_11-Apr-97.pdf, p.7). However, in Monsanto's petition to increase certain glyphosate tolerance levels in 2002, the EPA stated that it still did not have common mechanism of toxicity data for glyphosate (EPA, Mar. 2002).

Glyphosate and its metabolite AMPA have similar toxicological profiles and both have, until recently, been accepted by government and international health, environmental and regulatory agencies and organizations as generally safe (Monsanto, 2015; WHO, 2004). According to an EU website, a significant factor in determining its current safety is its mode of action—which, in glyphosate works by disrupting the synthesis of the enolpyruvylshikimate-3-phosphate (EPSP or shikimate pathway) where it blocks the EPSP from catalyzing the synthesis of, basically, essential plant metabolites such as the aromatic amino acids phenylalanine, tyrosine and tryptophan (which are also essential amino acids for humans). The website also explains that the mainstream assumption has been that the shikimate pathway does not exist in mammals, including humans, so glyphosates enzymatic disruption would not physically impact mammalian biological systems; however, according to the information provided on the website, that assumption does not include consideration that the shikimate pathway also exists in bacteria (http://www.glyphosate.eu/glyphosate-basics/how-glyphosate-works).

A review of a multitude of studies in the last fifteen years has revealed that human beneficial gut bacteria rely on EPSP synthesis and that glyphosate has been shown to inhibit that synthesis, thus potentially inhibiting critical amino acid synthesis that could, subsequently have a negative systemic impact on human and animal health. The authors link a host of health problems that could potentially stem from ingesting small amounts of glyphosate residue. (Samsel and Seneff, Apr. 18, 2013) However, this article is published in *Entropy*, and the publisher posted an "*Expression of Concern*" pointing out that the editors of the journal had received multiple complaints suggesting that the

authors used biased sources, but since “the nature of the claims against the paper concern speculation and opinion, and not fraud or academic misconduct” readers were offered a precautionary note (http://www.mdpi.com/1099-4300/15/4/1416).

By 2002, the EPA stated conclusively that glyphosate poses “no evidence of carcinogenic potential” (EPA, Mar. 2002, Sec. B,5; C,3,ii; C,4,iii;). The 2016 FAO/WHO report, confirming the non-carcinogenic status of glyphosate, stated that although it considered evidence of glyphosate formulations, “[t]he scope [of the evaluation] was restricted to the active ingredient” (http://www.fao.org/3/a-i5693e.pdf, p. 19). However, in the most recent re-registration of glyphosate, the EPA noted that it was “seeking toxicity data on formulated products containing the surfactant POEA, due to uncertainty about its risk to aquatic animals", but in the assessment report, there was no mention in the requirement about POEA toxicity tests in regards to human health (EPA, June 17, 2009).

In addition to the EPA’s established position that glyphosate is non-carcinogenic, the EPA recently concluded that glyphosate (independent of its adjuvant formulations) is not an endocrine disruptor (EPA, June 29, 2015). In the weight of evidence, the EPA (ibid) noted (as suggested in the study’s title) that they only considered research on the active ingredient rather than formulations with adjuvants. In order to conduct their assessment, the EPA (ibid) completed, in 2015, the first (Tier 1) of a multi-phase endocrine assessment project (that was supposed to be completed between 2004 and 2005 according to the Federal Food, Drug and Cosmetic Act, sec. 408(p)). A chemical passing Tier 1 (of which glyphosate was one) means it poses no risk to the endocrine system

(ibid). According to the EPA's recent Tier One Endocrine Screening Assays for glyphosate, "…glyphosate demonstrates no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways in mammals or wildlife" (Akerman and Blankinship, June 29, 2015, p. 26).

But how did Roundup get separated into active and inert ingredients in the first place? During the first decade of the EPA's existence, the high volume of pending pesticide registration called for a more efficient method of parsing out what could be considered safe, and therefore not requiring assessment, and what could be considered potentially hazardous. The EPA's solution was to classify certain substances, such as inert (or "other") ingredients that are used in various formulations, in graduated levels of hazard. By 1975, the GAO noted in their report that the Agency was only testing the active ingredient rather than the complete formulation and that the assessments of inert ingredients were weak (GAO, Dec. 4, 1975).

However, the International Program on Chemical Safety (IPCS) evaluation of glyphosate in 1994 concluded that although rodent studies indicated "a low acute toxicity by the oral and dermal administration routes [t]he role of adjuvants in the toxicity of glyphosate formulations needs to be investigated further in laboratory mammals and organisms in the environment" because "[t]he formulation Roundup is acutely toxic to humans when ingested intentionally or accidentally. No controlled studies are available and therefore the human NOAEL cannot be derived" (but IPCS made interim recommendations that suggested the use of protective clothing and the need for "a market based survey" to better estimate exposure rates of the general public)

(http://www.inchem.org/documents/ehc/ehc/ehc159.htm). The EPA, in 1995, however, published a notice in the Federal Register detailing a list of inert ingredients that were "reviewed by the Structure Activity Team of EPA's Office of Pollution Prevention and Toxics…and evaluated by the Office of Pesticide Program's Inert Review Group" (EPA, Jul. 7, 1995, p. 35397). The inert ingredients in this list, including polyethoxylated tallowamine (POEA)—a common ingredient in Roundup formulations—had been determined to be minimal risk to human health and were therefore reclassified from the List 3 (unknown toxicity) to the List 4b in which the EPA asserts that they have "sufficient information to conclude that [its] current use pattern in pesticide products will not adversely affect public health and the environment" (ibid). (See Appendix 6 for toxicity chart). At the time, Roundup (of which some claim that the majority of Roundup formulations utilize POEA's) had been registered for over twenty years. Roundup's versatility as a defoliant and plant growth regulator made it one of the leading pesticides in the world—even prior to the introduction of the first Roundup Ready crop (Székács and Darvas, 2012 (http://cdn.intechweb.org/pdfs/25624.pdf). However, recall that in 2015, glyphosate was reclassified (as discussed in Data Access Restrictions), again, back to List 3 (EPA, Sept. 15, 2015).

The 1993 RED included reference to §156.10 – Labeling Requirements under Title 40 of the Code of Federal Regulations, which states that "[t]he Administrator may require the name of any inert ingredient(s) to be listed in the ingredients statement if he determines that such ingredient(s) may pose a hazard to man or the environment" (EPA, Sept. 1993, p. 196). Monsanto (April, 2005) stated, in a letter responding to a study on

Roundup toxicity in aquatic systems, that "[i]t is misleading…to suggest that 'Roundup' and 'glyphosate' are synonymous" (p. 4). Monsanto further explained that most Roundup formulations contain a surfactant and that it is "inappropriate to attribute the effects observed [from surfactants] to glyphosate" (p.4). A 1979 study on the aquatic impact from glyphosate, Roundup and its surfactant, MON 0818—POEA, (which Monsanto's April, 2005 letter referenced to support its argument), stated that "[t]oxicities of the surfactant were similar to those of the Roundup formulation" (Folmar, Sanders and Julin, 1979, p. 1). In 2005, the EPA's Environmental Fate and Effects Division review of a study on amphibians that included glyphosate with one of the most common surfactants used herbicide applications—Polyethoxylated Tallowamine (POEA), stating that "the [e]ffects on metamorphosis, gonadal morphology and thyroid hormone gene expressions, suggest that POEA and glyphosate formulations containing POEA can impact endocrine-mediated processes" (Howe, et al, Aug. 2004, abstract). In addition, an EPA memo validated an Australian frog study on the effects of glyphosate and a Roundup formulation that found Roundup formulations more toxic than glyphosate alone (Oct. 1985). As early as 1985, according to one article, the EPA reviewed and commented on a study conducted by Folmar, Sanders and Julin (1979), and reiterated in 1997, that "the surfactants increased the toxicity of the product" (McLane, Apr 17, 1997). Another study that was reviewed by the EPA concluded that the surfactant, POEA, was not only toxic itself, but combined with glyphosate multiplies the toxicity of both active ingredient and surfactant (Carey, et al, Oct. 7, 2008).

In the E.U., pesticides registrations are, like in the U.S., granted for a limited time before they are required to be reassessed. And, like the U.S., assessment is conducted on the active ingredient. On June 19, 2013, the Glyphosate Task Force, a compilation of the agro-chemical manufacturers who originally applied for glyphosate approval, requested that Germany be the Rapporteur Member State (RMS) to conduct the assessment (N.A., June 19, 2013). (Germany was also the RMS that conducted the previous assessment in 1995.) Based on EFSA (2015) description of the RMS report, Germany assessed whether the dossier submitted by the Glyphosate Task Force was complete. Based on Germany's assessment and recommendations, the EFSA determined it was necessary to "seek expert consultation" for certain toxicological studies, the conclusion of which all but one of the peer review experts agreed that "glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential according to the CLP Regulation" (EFSA, 2015, p. 11). (CLP regulation is based upon EC 1272/2008—discussed above in Developing Standards: Harmonizing Roundup/glyphosate.)

The IARC Monographs, of which the controversial glyphosate review is a part, are a collection of studies conducted by interdisciplinary scientists that "review the published studies and evaluate the weight of the evidence that an agent can increase the risk of cancer" (http://monographs.iarc.fr/). After the WHO's IARC panel published their glyphosate assessment (IARC, 2015) which concluded that glyphosate is a "probable carcinogen", the EFSA called on the Rapporteur Member State (Germany) to consider IARC's research in its assessment. Germany's BfR (German Federal Institute for Risk

Assessment) carried out the review and submitted their draft report to EFSA. According to the BfR, the review consisted of 150 new and 300 previous toxicology studies on glyphosate as well as approximately 200 journal publications, the results of which, BfR concluded, indicated that glyphosate is non-carcinogenic, non-terratogenic and non-toxic to the reproductive system, although a reference list, specifying which studies were part of the assessment, was not provided in this report (http://www.bfr.bund.de/en/the_bfr_has_finalised_its_draft_report_for_the_re_evaluation_of_glyphosate-188632.html). The BfR stated that their studies also included a look at the adjuvants that make up some formulations of glyphosate and concluded that "there is convincing evidence that the measured toxicity of some glyphosate containing herbicides is the result of the co-formulants in the plant protection products (e.g., tallow-amines used as surfactants)" (ibid). BfR followed up this discovery by examining the results of one study that examined a glyphosate-containing herbicide (not specified in their summary), initiated by the BfR and conducted by the University of Veterinary Medicine in Hanover (ibid). BfR states that this study suggests that glyphosate is not disruptive to the gut flora of ruminants (ibid).

The BfR submitted their assessment and recommendations to the EFSA. In the BfR's summary of their assessment, they stated "[a]fter sending the draft re-assessment report of glyphosate to EFSA, it will constitute the basis for the public consultation with all interested stakeholders as well as for the so-called "peer review procedure" by experts from other EU member states" (BfR, Apr. 4, 2015). After reviewing IARC's study, the BfR suggested that their comments on the IARC report would be "inexpedient" and

strongly recommends that all of the EU states and competent authorities, the EFSA, EC, ECHA (European Chemical Agency), WHO, IARC and JMPR (FAO/WHO Joint Meeting on Pesticide Residues) should, at various stages, be involved in discussing, assessing and finalizing conclusions regarding further approval of glyphosate. In this six paragraph, one-page summary, the BfR dedicated three paragraphs—half the page—to this recommendation. According to available public information, however, this recommendation was not carried out and the EFSA based their final assessment for the reregistration of glyphosate on the BfR's report (EFSA, 2015; http://www.bfr.bund.de/cm/349/bfr-contribution-to-the-eu-approval-process-of-glyphosate-is-finalised.pdf). The EFSA's conclusions, however, do not take into consideration the BfR's suggestion regarding the potential role that co-formulants play in measured toxicity in some pesticide formulations (although the EFSA did not recognize this as a data gap because, according to the EFSA, only the active ingredient was being evaluated) (EFSA, 2015). Shortly after the EFSA assessment was published, the EC formally requested that the EFSA provide a statement addressing the toxicity of POE tallowamines (a.k.a POEAs) "based on the toxicological evaluation of POE-tallowamine presented by the rapporteur Member State Germany in the context of the peer review of the active substance glyphosate" (http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2015.4303/epdf). Recently, in an addendum to the EU 2002 review of glyphosate, the E.C. stated that "a significant toxicity of POE-tallowamine (CAS No 61791-26-2), a substance frequently used as a co-formulant in plant protection products containing glyphosate, was observed on all

endpoints investigated" and a new regulation went into effect August 1, 2016, declaring that Member States shall ensure that plant protection products containing glyphosate do not contain the co-formulant POE-tallowamine (CAS No 61791-26-2) (EC. July 11, 2016; http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32016R1313).

Data Details and Interpretations

Portier, et al (Mar. 3, 2016) stated that the BfR's recent glyphosate assessment lacked scientific rigor by dismissing statistically significant data, dismissing valid and relevant epidemiological studies and neglecting OECD guidelines in interpreting chronic and carcinogenicity studies. The EFSA letter responded to the points made by Portier, et al (Mar. 3, 2016) refuting each claim of weak scientific rigor, emphasizing that the IARC assessment was a great "first step" but that "we should not compare this first screening assessment with the more comprehensive hazard assessment done by authorities such as EFSA, which are designed to support the regulatory process for pesticides in close cooperation with the Member States in the EU" (EFSA, Jan. 13, 2016, p. 1).

In 1986, the EPA produced the first Reregistration Eligibility Decision (RED) for glyphosate and in the reference section of that document one can find several studies conducted in the early to mid-1970s. A 1977 memo regarding Monsanto's petition, to amend certain pesticide tolerance levels, referenced several industry studies (e.g. acute, dermal, reproductive, etc.) including two two-year studies (rat and dog). However, according to the EPA, in setting tolerances, the EPA criteria is based off of the acute toxicity NOEL's (EPA, Feb. 2, 1977). Using these studies, the EPA approved an increase in tolerance for several commodities from .05 to .1 ppm (corn grain was included in the

amended tolerance) (ibid). During the review process in 1985, the EPA's Toxicology Branch AD Hoc Committee reviewed Monsanto's glyphosate carcinogenicity study on mice, one on rats and a chronic study on beagle dogs. Upon review of these studies, the Review Committee noted that there were changes in the pituitaries of the beagles in the dog study for which the EPA requested additional data to "address findings in this study" and provided Monsanto (the registrant) a 50-month timeframe to submit the data (EPA, June 1986, p. 83). In the meantime, the EPA allowed a tentative pesticide residue NOEL (no observed effect level) of 20 mg/kg/day (ibid). The rat study, according to the EPA, revealed no significant chronic toxicity concerns, but the study needed to be re-done to include higher dosages so as to reach a maximum tolerance level.

The mouse study, however, revealed a rare type of tumor in the male mice. In an exchange of memos between Monsanto and the EPA, Monsanto claimed that the tumors that showed up in the mouse study were not related to the treatment but were rather examples of false positives that should be disregarded. However, one of EPA's Toxicological Branch's statistician's response to Monsanto referred to the statistical data and provided a detailed explanation, based on the data, why "a prudent person would reject the Monsanto assumption that Glyphosate dosing has no effect on kidney tumor production" (Lacayo, Feb. 26, 1985) (See Appendix 4 for EPA memos related to this issue). The following month, a group consensus review from the EPA's Toxicological Branch discussed the data and concluded, as summed up by review member, William Dykstra (Mar. 20, 1985) that "[g]lyphosate has been identified as an oncogene in male mice. A dose-related increase in renal tubule adenomas was found. These tumors are

considered compound-related". The study on mice showed kidney tumors and the Review Committee declared glyphosate a Group C carcinogen ("limited evidence that it can cause cancer in animals in the absence of human data, but at present it is not conclusive) and the Agency determined that the studies needed additional review (Farber, et al. Mar. 4, 1985; http://www.greenfacts.org/glossary/def/epa-cancer-classification.htm).

The studies were then reexamined by the Federal Insecticide, Fungicide and Rodenticide Act's (FIFRA's) Scientific Advisory Panel (SAP) which found that although the mouse study showed significant results compared to historical control evidence (which suggests that previous studies were used in comparison) they determined that such significance was overridden by the current study control group's lower survival rate than its high-dose test group. In addition, the SAP stated that the maximum tolerated dose (MTD) had not been achieved in the rat study and the significant differences in dose levels between the mouse study and the rat study (the rats were given approximately 1/100 the dose of the mice) made the two incomparable, rendering evidence to determine carcinogenicity inconclusive. Therefore, they determined glyphosate as a Group D carcinogen ("inadequate animal evidence of oncogenicity"), requesting that the mouse and rat studies be repeated and submitted (also within a 50-month timeframe) to address protocol standards and reach MTD, respectively (EPA, June 1986).

A second mouse study was never submitted, but a second rat study was conducted and in 1991 (after multiple review panels discussed not only the rare tumors found in the mouse studies, but also the potential significance of the high rates of pancreatic adenoma that occurred in the rat study) the findings were reviewed by the Health Effects Division

Carcinogenicity Peer Review Committee which subsequently classified glyphosate as a Group E pesticide, indicating that there is strong evidence of non-carcinogenicity "based upon lack of convincing carcinogenicity evidence in adequate studies in two animal species" (Dykstra, Oct. 30, 1991, p.i). The review committee went on to clarify that "[i]t should be emphasized, however, that designation of an agent in Group E is based on the available evidence at the time of evaluation and should not be interpreted as a definitive conclusion that the agent will not be a carcinogen under any circumstances" (Dykstra, Oct. 30, 1991, p. i). The 1993 RED reiterates this precautionary note, reminding registrants that, in regards to the registered pesticide, if they obtain "any factual information…from whatever source, including but not limited to interim or preliminary results of studies, regarding unreasonable adverse effects on man or the environment" the registrants must notify the Agency per requirements of FIFRA section 8(a)(2) (EPA, Sept. 1993, pp. 225-226).

Six of the 1993 RED studies (out of over 100 studies listed) were chronic and/or carcinogenicity studies, two of which were albino rat studies that were not described within the chronic/carcinogenicity section. In addition to the six chronic and/or carcinogenic studies listed in the 1993 RED, an Addendum was mentioned in the reference section regarding the pathology assessment for the initial study on mice, and, although I was not able to locate the addendum in the EPA archive database, it coincides with a follow-up memo that discussed the results of further review of the existing tumor samples as well as three more samples taken from each of the affected mice (ibid). Under the "Data Supporting Guideline Requirements for the Reregistration of Glyphosate"

section in Appendix B of the 1993 RED, the two albino rat studies are mentioned in reference to supporting data for the oncogenicity – rat" requirements (EPA, Sept. 1993). In addition, it was stated that one of the albino studies also was used to support the "chronic feeding toxicity—non-rodent" requirements (ibid). In addition to that, a 21-day dermal toxicity study on rabbits was listed as supporting data for the chronic feeding toxicity studies for rodents (ibid). (According to OECD guidelines, dermal toxicity tests are administered on the skin, not in food (http://www.oecd.org/chemicalsafety/risk-assessment/1948333.pdf)). According to the EPA MRID numbers, the EPA's latest IRIS statement summarized the same dog study and the original rat study as the 1986 and 1993 REDs, with the addition of a higher dose Rat study (that was reviewed in 1991 to address gaps in the 1986 RED data), as key studies supporting current assumptions of safety and regulatory decisions (https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0057_summary.pdf; EPA, June 1986). (According to the EPA, "[a]n MRID is unique eight-digit number assigned to each study submitted to EPA") (https://www.epa.gov/pesticide-registration/study-formatting-and-supplemental-information). The incidences of tumors in the mice and rat studies were determined as either insignificant or were considered to be not conclusively connected to the effects of the treatment (EPA, Sept. 1993; EPA, June 1986; see Appendix D to view the follow-up memo) The additional beagle study data that was requested in the 1986 RED was apparently satisfied, instead, with an addendum from Monsanto to the EPA rationalizing why the pituitary weight changes were not related to the treatment (Dykstra, Jan. 12, 1987). The 1993 RED deleted the

brief discussion regarding the pituitary changes and replaced it with a statement that the study "showed no effects based on all parameters examined" and the NOEL was raised from 20 to 500 mg/kg/day (EPA, Sept. 1993) (see Appendix 5 for EPA memos related to this study). The overall outcomes summarized in the chronic toxicology section of the 1993 RED highlighted data that the EPA considered demonstrative of minimal short or long-term toxicity risk to humans (ibid).

However, in 2008, Gilles-Eric Séralini and Nora Benachour submitted the results of an in vitro study on glyphosate Roundup formulations and AMPA which used three different types of human cell types—placental, embryonic and umbilical cord. In 2009, Benachour and Séralini took part in a study analyzing the effects of Roundup formulations on liver cells (Gasnier, et al., June 17, 2009). The results of these tests according to Benachour and Séralini (2009), "clearly confirms that the adjuvants in Roundup formulations are not inert" and that they are endocrine disruptors and potentially carcinogenic (p.97). But in vitro studies are controversial too and industry scientists and researchers, according to an article on Monsanto's website, have countered that testing cells in a petri dish inadequately represents the impact substances have on cells within a complex biological system (http://www.monsanto.com/products/documents/glyphosate-background-materials/bkg_richard_response_2005.pdf).

Prior to Séralini's study, the U.S. and OECD member countries emphasized the assumption that "[a] properly conducted 90-day subchronic test should provide a satisfactory estimation of a no [observed] effect level" (NOEL) (OECDb, Sept. 21, 1998,

p.1). According to the 13-week rat study submitted by Monsanto, the NOEL's for NK603 consumption focus on the effects of CP4 EPSPS protein levels that concluded there were no adverse effects observed at the highest dosage levels (572 mg/kg) (Hammond, Dudek, Lemen and Nemeth, Feb. 12, 2004). However, according to the studies Monsanto submitted for EPA pesticide tolerance level approval for glyphosate on corn (and other crops), the sub-chronic (90-day) toxicity NOEL of glyphosate for mice at 90 days was recorded at 10,000 mg/kg, while the chronic (2-year) toxicity NOEL was recorded at 750 mg/kg for mice and 362 mg/kg for rats (EPA, Dec. 24, 1996). However, in assessing the safety of glyphosate, the 2016 FAO/WHO report stated that "[t]he overall weight of evidence indicates that administration of glyphosate and its formulation products at doses as high as 2000 mg/kg bw by the oral route…was not associated with genotoxic effects in an overwhelming majority of studies conducted in mammal" (http://www.fao.org/3/a-i5693e.pdf, p. 21; http://www.monsanto.com/glyphosate/documents/no-evidence-of-carcinogenicity.pdf).

Reflecting on the divergent interpretations, of the mouse study (described above), between Monsanto and the initial EPA toxicological review panel regarding false positives, the European Environmental Agency (EEA) recently published an updated text that analyzes individual cases of regulatory "false positives" over the last 100 years in which a precautionary policy stance was favored over risk. The EEA concluded that of the 88 cases studied, only four turned out to be actual false positives. Of the other 84 cases, approximately one-third were considered "real risks", approximately one-third were considered scientifically ambiguous, i.e. "the jury is still out", and the other third

were a combination of “unregulated alarms”, “too narrow a definition of risk”, and “risk-risk tradeoffs” (http://www.eea.europa.eu/publications/late-lessons-2, p. 17). Jamieson, Oreskes and Oppenheimer (Jan. 2005) state that “there is an almost universal horror of false positives. Thus, standard statistical methodologies permit an investigator to miss real effects in order to avoid claiming an effect that does not actually exist” (p.55).

Caution as it is used here, however, is relative to what is being protected. Jamieson, Oreskes and Oppenheimer (Jan. 2005) go on to explain: “In reality, this may have as much to do with our statistical practices…as it does with whether the effect is actually present. Yet the failure to scientifically demonstrate an effect is often interpreted as showing that the effect does not exist” (p.56). Needleman and Gee (2013), concur, stating that “'[n]o evidence of harm is thereby mischaracterised as 'evidence of no harm'” when faced with a lack of adequate, valid or convincing data for conclusive scientific interpretations (p. 50).

Conflicts of Interest and Public Trust

In the 1980’s, Ashford (1984) discussed that there were significant flaws in how the EPA selected its Scientific Advisory Panels/Boards, stating that the selection process allowed for an unbalanced, industry-weighted scientific review of widely-used (but potentially toxic) chemicals that put the EPA at risk of inadequately protecting the public and environment from chemical hazards by relying on industry-supplied data and industry-favored assessment. A June 2001 GAO report, which focused on analyzing criminal financial conflict of interest statute and the Office of Government Ethics conflict of interest regulations, stated that the EPA had yet to develop a system to request and

collect essential information to determine the independence, balance of viewpoints and conflicts of interest of their Board Reviewers. In addition, the GAO report noted that public access to appropriate and sufficient information regarding the panelists' background and "points of view represented on the panels" was inconsistent (p. 21). This report reviewed four Science Advisory Board panels (between 1997 and 1999) that were selected to review the "EPA's Guidelines for Assessing the Health Risks of Carcinogens" (p. 34). The EPA stated that it sought to create a "broad middle" perspective in which the majority of panelists were university researchers serving as a bridge between industry and environmental protection interests, but the GAO pointed out that the EPA's initial inadequate collection of financial and professional interest information illustrated how the perspective of this balance could shift when the GAO incorporated critical information necessary for a more complete background for each panelist. The GAO report stated that the EPA "would be better able to assess panelists' impartiality and ensure that panels are properly balanced if it had an understanding of the work performed by the panelists for law firms and industry, particularly for chemical companies" (p. 10). The GAO listed the panelists in four separate tables, according to the review panel in which they were participating, categorized according to whether they were explicitly affiliated with a university, industry, or the EPA. Figure 1 compiles the GAO tables. The GAO then provided additional information that, according to the GAO and EPA, would have altered the composition of the "broad middle" and industry categories. According to the report, the EPA agreed with the GAO assessment—that consistent and thorough financial (and professional affiliation) background information collection, retention and

dissemination would help better ensure a more balanced and transparent scientific review process.

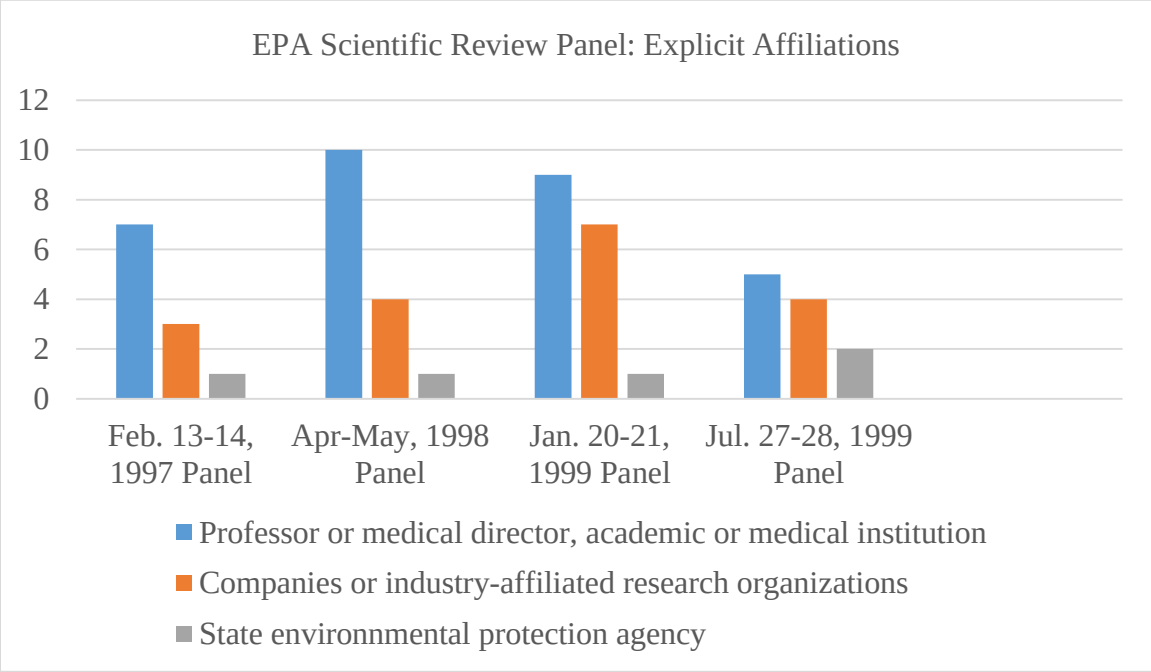

Figure 1. EPA Scientific Review Panel: Explicit Affiliations Prior to GAO Adjustments.

The EU has also been subject to recent scrutiny regarding conflicts of interest in the EFSA. In 2010, Nikiforos Diamandouros—former European Ombudsman—followed up on a complaint regarding a former Head of EFSA's Genetically Modified Organisms Unit (Suzy Renckens) who left the EFSA in 2008 and less than two months later took up the position of Head of Biotech Regulatory Affairs for Europe, Africa and the Middle East for Syngenta (http://www.ombudsman.europa.eu/en/cases/recommendation.faces/en/11089/html.bookmark). Diamandouros recommended that the EFSA address its lax conflict of interest policy (http://europa.eu/rapid/press-release_EO-11-20_en.htm). In 2010, the EFSA demonstrated that it had not addressed the Ombudsman's concerns as the Chairwoman of

EFSA's Management Board, Diáná Bánáti, was asked to resign after her concurrent membership on the board of an international biotechnology lobby group (ILSI) was made public. Bánáti is now the Executive Scientific Director of ILSI. On the other hand, the executive director of EFSA, in 2010, raised concern with a member of the European parliament's budget committee's involvement with a prominent environmental NGO (http://www.europarl.europa.eu/sides/getDoc.do?type=REPORT&reference=A7-2012-0106&language=EN&mode=XML; http://www.bbc.com/news/world-europe-18007004

After the publication and retraction of Séralini, et al's (2012) study (on the chronic toxicity of NK603, a Roundup formulation and glyphosate) and the subsequent volume of conflicting media attention given to the outcomes of the study and speculation regarding the reasons for its retraction, the EC funded two projects, G-TWYST (GM Plants Two-Year Safety Testing) and GRACE (GMO Risk Assessment and Communication of Evidence) and France funded GMO90+. Each of the projects offer websites that openly describe the purpose, parameters, design and funders. Both G-TWYST and GRACE provided opportunity for public input during the planning stage, suggesting a certain level of access and influence in the project. The GMO90+ project complements G-TWYST in that it will use the same food (NK603) and same rat strain. GMO90+ will conduct 90-day and six month studies in an effort to discover "predictive biomarkers" that could help make 90-day studies more accurate and effective (http://www.rechercheriskogm.fr/en/actualites#106). The study, according to their website, is in progress. G-TWYST is the E.C. replication of Séralini's study but with a larger number of rats. It is designed to "[clarify]…uncertainties raised through the

outcomes and reports from [Séralini, et al's, 2012 study]" and help further determine whether long-term feeding studies are necessary for risk assessment and policymaking—the study, scheduled to begin August, 2015, apparently has not begun yet (http://www.g-twyst.eu/news). The GRACE design is two-fold. One half of the project was to analyze systematic reviews and evidence maps as possible strategies to "identify, analyze and communicate primary research data on potential impacts of GM crops and their products on human and animal health, the environment and socio-economic indicators in a transparent, reproducible and unbiased manner" (www.grace-fp7.eu). The other half of the GRACE project was a 90-day rat study with MON810, using its closest conventional counterpart as a control. The results of the systemic/map study indicated that such reviews and approaches could provide useful data for risk assessors/managers in regards to gaining a better understanding of the impacts of genetic modifications. According to GRACE results, the rat study confirmed previous studies that concluded that the 90-day test on MON810 did not produce significant differences between control and test groups (ibid). The Austrian Federal Ministry of Health, however, wrote a letter to GRACE that highlighted several points in both parts of the projects that conflicted with their interpretation of how the study should have been designed, conducted and interpreted. GRACE responded, offering an explanation for each point (http://www.grace-fp7.eu/en/home).

In searching for public opinion regarding POEA's, a Google search using the key words "Roundup POEAs public opinion" and "Roundup inert news" offers a multitude of articles and websites with titles such as "Weed-Whacking Herbicide Proves Deadly to

Human Cells (http://www.scientificamerican.com/article/weed-whacking-herbicide-p/); "Here's Why 'Inert' Ingredients May Be the Most Harmful of All" (http://articles.mercola.com/sites/articles/archive/2016/05/31/roundup-inert-ingredients.aspx); "The Great Glyphosate Debate" (http://northernwoodlands.org/articles/article/the-great-glyphosate-debate) and others. In addition, a group of over 100 scientists recently petitioned Green Peace to stop opposing genetically engineered crops, stating in their letter that,

> [s]cientific and regulatory agencies around the world have repeatedly and consistently found crops and foods improved through biotechnology to be as safe as, if not safer than those derived from any other method of production. There has never been a single confirmed case of negative health outcome for humans or animals from their consumption. Their environmental impacts have been shown repeatedly to be less damaging to the environment, and a boon to global biodiversity. (http://supportprecisionagriculture.org/nobel-laureate-gmo-letter_rjr.html; https://www.washingtonpost.com/news/speaking-of-science/wp/2016/06/29/more-than-100-nobel-laureates-take-on-greenpeace-over-gmo-stance/)

The letter also referenced the need to feed a growing global population and elaborated on the potential benefits of "Golden Rice" as a means to alleviate vitamin A deficiency in developing countries. Green Peace responded:

> Golden rice has failed as a solution and isn't currently available for sale, even after more than 20 years of research…Rather than invest in this overpriced public

relations exercise, we need to address malnutrition through a more diverse diet, equitable access to food and eco-agriculture. (https://www.washingtonpost.com/news/speaking-of-science/wp/2016/06/29/more-than-100-nobel-laureates-take-on-greenpeace-over-gmo-stance/)

Integrative Research

A multitude of research studies have analyzed and assessed the interactions of glyphosate and transgenic crops independently. But fewer studies have integrated glyphosate, glyphosate formulations, such as Roundup, and herbicide tolerant crops, such as NK603. According to Séralini's, et al (2012) article, the purpose of their study was to expand on the 90-day (sub-chronic toxicity) study that Monsanto (referred to in their article as "the petitioner") had conducted by not only extending the length of the study to two years but also exploring more parameters. The reason to conduct a long-term study, according to Séralini, et al (2012) was because Monsanto's conclusion, that there was no significant difference between the control and test outcomes, conflicted with subsequent independent studies that suggested otherwise. In a follow-up article, Séralini clarified that their study adhered to the 1981 OECD 452 guidelines, which, according to the authors, were the guidelines "in application when the study started in 2008" (Séralini, et al(b), 2012, p. 477). OECD guideline 408 is what Monsanto used to design its 90-day (sub-chronic toxicity test) study from which Séralini and his team replicated and/or expanded on (in terms of matching rat type and number, feed type, dosage levels and parameters measured) (Séralini, et al, 2012).

In addition to rodent/animal toxicology studies, academic and U.S. agency researchers with the USDA have conducted significant studies on conventional and transgene crops and the impact of glyphosate on plant and soil microbiology (e.g. Kremer, Means and Kim, 2005; Barrow, Lucero, Osuna, Reyes and Aaltonen, Aug. 1, 2007). Dr. Huber (personal communications, May 23-June 7, 2016) had been working with a team of senior plant and animal scientists who discovered a potentially new, potentially devastating plant pathogen that appeared directly linked with transgenic crops and the impact of glyphosate interactions within plants and soil. Initial results of their studies suggested that this new pathogen not only negatively affected plants (e.g. potentially causing or contributing to Sudden Death Syndrome in soy and Goss' wilt in corn) but also mammals (e.g. potentially causing or contributing to miscarriages and spontaneous abortions in cows and pigs) (ibid).

Huber was seeking precautionary action from U.S. Secretary of Agriculture Tom Vilsak, asking the USDA to hold off on its approval of GM-alfalfa. Huber was also seeking support for further research into these initial findings (which suggested a potential negative impact from glyphosate mineral chelation on GMO and non-GMO plant nutrient uptake which, in turn, contributes to weakening its immune system and making the plant more susceptible to disease, thus creating an inviting environment for bacterial and viral growth and the introduction and spread of a newly discovered pathogen). In addition to this, what also alarmed Huber was the potential widespread hazardous impact that this pathogen could have on agricultural crops, animals and humans, when one considers the extent to which glyphosate is used for transgenic and

conventional crops. In his letter to U.S. Secretary of Agriculture Tom Vilsack, Huber (Jan. 17, 2011), explains that although the consequences of this newly discovered plant pathogen (linked to glyphosate/Roundup) “could result in a collapse of US soy and corn export markets and significant disruption of domestic food and feed supplies”, inaction regarding further research to appropriately address the issue could potentially create “a general collapse of our critical agricultural infrastructure”. Huber’s request to USDA Secretary Vilsak for interagency support to conduct further research has been, according to Huber (personal communication, June 5, 2016) “essentially ignored”. Huber stated, however, that the research has continued—without federal support—and they have completed preliminary analyses which confirm the existence and negative impact of this new pathogen on plants and mammals (personal communication, May 23, 2016). In addition to individually approaching USDA Secretary Vilsak by letter, Huber mentioned that “[a] group of us scientist have met with the various agency heads (Vilsack has never been available, but assistants have) to share our findings and 135 or so peer-reviewed scientific papers, but to no avail (comments like "When you get more information, please contact us.")” (ibid).

Another highly credible scientist, Dr. Robert Kremer, had also been researching soil and plant pathogens and discovered similar outcomes in terms of glyphosate playing a role in creating an environment conducive to hazardous bacterial and pathogen accumulation. Through direct email communication, Dr. Robert J. Kremer (personal communication, June 2-6, 2016) provided the following material regarding his work and experience working with the USDA as it pertains to the questions I posed to him (See

Appendix 8). Dr. Kremer spent the latter half of his career (approximately seventeen years) researching soil microbiology and the role that glyphosate plays in microbial soil and plant interactions. Kremer noted that when he began this research, the first transgenic crop (soy) was just entering the market and even though researchers already knew that glyphosate predisposed susceptible plants to heavy colonization and infection of roots after application (due mainly because glyphosate is systemically transferred throughout the plant and that the mode of action leads to inhibition of the plant's defense mechanisms), no one had reported the possibility of similar occurrence in the resistant transgenic soybean varieties (Kremer, personal communication, June 2, 2016). In other words, according to Kremer, the researchers collaborating in the USDA and the University of Missouri project were the first to study this topic. When funding was cut for the collaborative project and Kremer continued this research under the umbrella of his existing USDA project, Kremer noted that he and a fellow microbiologist colleague "were the only researchers in the agency working on the glyphosate-transgenic crop effects on biology; however, several other researchers were working on the transgenic crops from a production standpoint" (June 2, 2016).

According to Kremer, an initial study (Kremer, Means and Kim, 2005) suggested, and subsequent field trial studies confirmed, that unintended effects of transgenic modifications seem to contribute to the plant roots releasing an excess of carbohydrates and amino acids which is "related to the abundant colonization and infection of the roots by soilborne fungi (Fusarium spp.)". Glyphosate seems to be related to this process as it travels through the plant to its roots, where it is released into the soil. Because it binds

tightly with the soil, it does not travel far from the plant roots. Contrary to INCHEM's 1994 glyphosate assessment concluding that the results of "field studies…support the view that glyphosate does not affect soil microorganisms in the long term" (http://www.inchem.org/documents/ehc/ehc/ehc159.htm), Kremer's (personal communication, June 3, 2016) research demonstrated that whether a plant is designed to withstand the effects of glyphosate or not, the unintended effect created by the presence of glyphosate, as indicated by the consistent increase in harmful bacteria colonization, increases the potential to weaken not only the roots, but the plant as a whole.

Another retired USDA microbiologist, Dr. Mary Lucero described a moment of her own scientific revolution as she began working on soil microbiomes with the USDA and realized that what had previously been her theoretical foundation of reality regarding how plants thrive in a given environment was turned upside down as she physically worked with plant and soil microbiomes. What she realized is that her previous theoretical assumption that plants grown in vitro required a sterile environment to avoid disease was essentially backwards as she realized that plants and soil contain and depend on millions of microbes. Not all microbes are beneficial, of course, but Lucero's research uncovered the vast potential that beneficial microbes could have on plant and soil vitality (https://www.youtube.com/watch?v=UDLdTXe2koo; Lucero, et al, 2014; Lucero, Barrow, Osuna and Reyes, Mar. 16, 2008; Lucero, Barrow, Osuna and Reyes, Apr. 2006).

In 2012, a group of USDA researchers, according to Kremer, conducted a review (that included much of his research) which concluded that the "evidence of the impacts of

glyphosate is limited or not supported" (personal communication, Kremer, June 2, 2016). In a follow-up email, Kremer elaborated that the scientists who reviewed his work are "traditionalists", some of whom, from his perspective, "seek to explain results based on classical mechanisms" rather than broaden their theoretical boundaries (personal communication, Kremer, June 3, 2016). In other words, Kremer suggested that "[some] still dismiss the ability of an applied chemical pesticide to cause "unexpected effects", such as glyphosate promoting proliferation of certain microorganisms in the root zone" (ibid).

As Lucero's research evolved and began demonstrating consistent results, and as she began to share those results, she noted a significant shift in agency support—invisible boundaries that she had not realized she was working within until her research uncovered groundbreaking data demonstrating how to reduce or eliminate synthetic pesticides and extensive irrigation by balancing soil microbiomes. She explained that the USDA had supported her research while her data was still suggestive but when she began to confirm her initial findings with consistent numbers that demonstrated the validity of her hypothesis, within weeks she was told by a national [USDA] program leader that her work, because it did not support agricultural chemical companies, would never be supported by the USDA (https://www.youtube.com/watch?v=UDLdTXe2koo, 4.35).

Dr. Kremer and Dr. Lucero spoke favorably of the USDA, emphasizing that for the majority of their careers they felt well-respected by their superiors and by the Department in general and were given a fair amount of flexibility and authority over their research projects. However, a basic, mainstream search online for Huber's, Kremer's and

Lucero's work (discussed above) provides an abundance of anti-GMO chatter regarding a few interviews or statements that the researchers had made that could be easily paraphrased in support of an anti-GMO cause, but in regards to professional and regulatory discussion regarding their work, the landscape is relatively barren compared to the time and space given to justifying glyphosate and GE crop safety.

The experiences of the scientists mentioned above are noteworthy, particularly in context with a statement made by the Office of Management and Budget (2002) regarding a "basic standard of quality for the use of science in agency decisionmaking":

> Under 42 U.S.C. 300g—1(b)(3)(A), an agency is directed, "to the degree that an Agency action is based on science," to use "(i) the best available, peer reviewed science and supporting studies conducted in accordance with sound and objective scientific practices; and or best available methods (if the reliability of the methods and the nature of the decision justifies use of the data). (p. 8457)

Cultural Perceptions

Contrary to U.S. pro-agricultural biotechnology policies, the European Union has integrated the Precautionary Principle into their legislative decision-making process, which requires, as the title suggests, a level of caution in assessment and decision-making processes. The Precautionary Principle, which is written into EU Treaty on the Functioning of the European Union and referenced throughout EU legislation, is defined as:

> The precautionary principle enables rapid response in the face of a possible danger to human, animal or plant health, or to protect the environment. In

> particular, where scientific data do not permit a complete evaluation of the risk, recourse to this principle may, for example, be used to stop distribution or order withdrawal from the market of products likely to be hazardous. (http://eur-lex.europa.eu/legal-content/EN/TXT/?uri= URISERV % 3Al32042)

Although some proponents of agricultural biotechnology suggest that the European Union's precautionary stance is based on conjectural risk, meaning that there is no convincing evidence of current, tangible risk that would justify precautionary action—that such precaution is based on a type of imaginary fear—many European government representatives are not convinced that the scientific evidence presented by industry or industry-backed organizations/institutions is complete or convincingly valid (EC, 2011). The U.S. has filed legal complaints, within the context of international trade agreements, against the E.U. for what the U.S. considers unsubstantiated bans and restrictions on E.U. GMO imports. WTO disputes between the U.S. and the E.U. over E.U. member country moratoriums on (and independent member country resistance to) GMO imports from the U.S., Canada and Argentina have resulted in the U.S. (along with Canada and Argentina) filing complaints against the E.U. The EU defended its actions by claiming potential health and environmental hazards of GMO's warranted a precautionary approach. But the WTO panel reviewing the case determined that the EU had acted "inconsistently with its obligations" to WTO agreements and that the EU's actions "should take into account risk assessment techniques developed by the relevant international organisations and be made on the basis of scientific principles" (http://www.ictsd.org/bridges-news/biores/news/eu-ministers-give-green-light-to-national-gmo-crop-cultivation-bans).

Multiple public polls conducted between 2003 and 2015 from the Pew Research Center consistently indicate that a majority of adults both in the U.S. and Europe considered genetically modified food unsafe (http://www.pewresearch.org/topics/health/). Multiple newspaper articles highlight persistent tension between public concern for food safety and industry and government assurance that the current food system is safe and all sides are using scientific knowledge, to an extent, to justify the basis of their claims. The following references are simply a few examples of the some of the mainstream public opinions, discussions and statements surrounding this conflict: (http://www.nytimes.com/topic/subject/genetically-modified-food; http://well.blogs.nytimes.com/2015/06/08/fears-not-facts-support-gmo-free-food/?_r=0; http://www.nytimes.com/2015/12/01/opinion/tell-consumers-what-they-are-eating.html; http://www.nytimes.com/2015/10/25/opinion/sunday/with-gmo-policies-europe-turns-against-science.html; http://www.nytimes.com/2014/01/09/opinion/gmo-foods-and-the-trust-issue.html; http://www.nytimes.com/2002/08/30/world/between-famine-and-politics-zambians-starve.html?pagewanted=all; etc.).

Conclusion

The 2016 U.S. National Academies of Sciences, Engineering and Medicine study emphasized that the issue of biotechnology, quoting the former (1999) Secretary of Agriculture Dan Glickman, “boils down to a matter of trust. Trust in the science behind the process, but particularly trust in the regulatory process that ensures thorough review” (National Academies of Sciences, Engineering and Medicine, 2016). The policy development for NK603 and Roundup is complex. It depends, in large part upon the

validity of the scientific methods that support the determination of whether a product is safe or not. How science is determined as valid is determined by the integration of a multitude of economic, socio-cultural and political factors that influence how knowledge is created, transformed and disseminated between researchers, industry, governments and the public. The conflict surrounding Eric Gilles-Séralini's et al (2012), research provides a window to the broader issues at stake with GMO policy development and pesticide regulation. The research presented here demonstrates that (in addition to stakeholder interests) transparency, trust, and balance of power are integral underlying factors driving conflicting ideologies and scientific interpretations of whether herbicide tolerant GMO's and their accompanying pesticides, are safe, or not.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

How do science and industry influence state-level policy and regulatory decision-making processes regarding the safety and/or promotion of a specific genetically modified corn (NK603) and the herbicide (Roundup) with which it is designed to work? How and what knowledge is generated and how is it transformed between scientists, industry and government to create policies and regulations for production and consumption of NK603 corn? What are the possible benefits/consequences of current safety protocols and how are those protocols met or challenged by Séralini's research team's study?

To answer these questions, I have analyzed major components of the agricultural biotechnology knowledge system including: significant legislative and regulatory policies and processes within the U.S. and the E.U., influential organizations and industries, a thorough review of a multitude of relevant industry and academic studies, interviewed two highly competent scientists from the public research field, and perused newspaper articles, websites and independent polls that provided a feel for overall public perceptions of agricultural biotechnology. The following discussion is arranged similarly to the preceding chapter, presenting my analysis of the research within the major themes that resonated throughout my research.

Theme 1: Developing Standards

Cultural Transitions

The research and discoveries of Cohen and Boyer were not only groundbreaking for the field of bioengineering, gene transfer technology and science in general, but they also introduced new potential environmental solutions as well as potential solutions for agriculture and healthcare industries, although public perceptions, scientific interpretations and government representatives were (and still are) divided on whether bio-agriculture represents positive benefits, devastating risks or something in-between. While increased crop yields were one marketing point, perhaps more significant for herbicide tolerant crops was the perception that glyphosate was a safer alternative to previously used herbicides. Thus, even though an increasing number of weeds have become resistant to glyphosate (which require increasing application rates as well as the number of times applied in a season), its use is justified as a better solution than using alternative, more hazardous pesticides. In order to create a viable market for genetically engineered foods, however, gaining public trust in agricultural biotechnology became an international priority for OECD member country representatives.

As Wald (1996) predicted, agricultural biotechnology has met challenges in how the public and researchers perceive the need for and safety of biotechnology, as is evidenced in the newspaper headlines and GMO-related websites, researcher studies and letters. The tension between resistance to and acceptance of new technology—especially technology that challenges cultural traditions—could be viewed as just part of the growing pains of a scientific revolution maturing into its own paradigm. But, U.S.

agricultural biotechnology is based on the success of "traditional" agriculture. The U.S, utilizing its skill and capacity to grow food has increasingly produced crop surpluses and has not, as a general populace, experienced the pang of hunger since the Dust Bowl era. Without the crisis of a broadly felt need to change how our food is made, there is decreased incentive to accept the risks of biotechnology. One could view this from a social construction perspective, in terms of cultural norms and boundaries of reality, in that without an applicable and wholly integrated societal need (real or perceived) for that technology, social processes will erect barriers to its implementation if other, more familiar methods are perceived as capable of meeting those needs. In other words, if the OECD wanted to pursue agricultural biotechnology as the next scientific revolution, it would have to discover or create a need sufficient to overcome societal resistance. In the meantime, industry and government had been working on regulatory procedures (e.g. substantial equivalence) that would make a smoother, faster transition from development to marketplace.

In order to fulfill the economic and political potential of agricultural biotechnology, both government and industry would need to establish a basis of safety. Establishing a basis of safety required that products meet a multitude of government approved safety criteria. Much of the criteria, test guidelines, regulatory processes and research data that led to the approval of NK603 was produced through international government and industry collaboration. The U.S. agenda to promote and become leaders of biotechnology and the public policy and regulatory development developed to follow that path that was conducive to reducing unnecessary regulatory barriers to agricultural

biotechnology innovation. Establishing a basis of need required a unique set of attributes distinct from and superior over existing products or technology. Perhaps by marketing for convenience, nutritional benefits, safety assurance and environmental benefits, increased production and decreased global hunger, Salomon Wald envisioned the basis for which agricultural biotechnology could potentially overcome public resistance.

The E.U. has found itself in a difficult situation in terms of making decisions that run contrary to certain socio-cultural aspects of member nations and economic sectors of the economy. As the U.S. is a major exporter and E.U. is a significant importer, E.U. bans and trade restrictions on GMOs, from this perspective, could be perceived as a threat to industry legal rights and regulatory freedom (as established by WTO and U.S. national policies) as well as marketing advantages of the exporter's national economy and its political power and status as an innovative leader. The WTO's determination that the E.U. cannot use the Precautionary Principal based on claims of safety , in a sense, indicates that the subject, as far as international trade relations is concerned, is now closed, regardless of how science and knowledge has evolved outside of the context of "risk assessment techniques developed by the relevant international organizations" (http://www.ictsd.org/bridges-news/biores/news/eu-ministers-give-green-light-to-national-gmo-crop-cultivation-bans). This is just one example of how (and which) data is used has the potential to impact international trade and human health. The WTO review panel decision has also created a legal barrier that inhibits expression of underlying cultural differences and alternative obligations (e.g. E.U.'s commitment to biological diversity as a signatory of the Cartagena Protocol). Without comparable agricultural

biotech-industry influence at the regulatory and policy making level that the U.S. has experienced, the E.U. political process seems more weighted in favor of public opinion, needs and interests, which run counter to certain harmonized trade rules. However, socially constructed values of how safety is perceived have been streamlined with WTO trade, OECD harmonization and U.S. regulatory processes. Perceptions of safety that run counter to those streamlined processes threaten the system in terms of delaying and/or inhibiting trade as well as diminishing the foundation that certain key products are a safe, viable commodity. To avoid continued conflict with the established rules and assumptions of safety, certain amendments in E.U. legislation have shown a shift in emphasis from protecting human health and, in some amendments, protecting cultural values, to incorporating an increasing focus on creating a "harmonized" system for domestic and international trade. The shift, noted in the language of certain amendments in European Commission regulations, indicates a level of transition from a more public health to private protection, which suggests that the conflict is not as simple as "us" versus "them", but integrated within the E.U. as well. Also integrated within the E.U. is tension between appealing to the standards of harmonized global trade and appealing to the unique needs and interests of its individual member states—needs and interests that are not adequately addressed in the WTO but persistent within E.U. society. Where some agricultural biotechnology supporters within the E.U. perceive the E.U.'s precautionary stance as a weakness that is hindering market and economic participation and success, others within the E.U. solicit alternative interests that frame the E.U. position as independently paced within its own cultural interests.

Defining Roles in the U.S.

Without an intervening step from seed development to field trial, the USDA - APHIS was able to pattern genetically engineered crop regulation in accordance to their pre-existing regulatory authority over conventional crops—in terms of plant protection. By the time Monsanto petitioned APHIS for NK603's non-regulated status, APHIS' role focused on the environmental impact of how plants would interact (particularly if they would alter the DNA of non-target plants and become a containment threat or if the bacterial and/or viral transgene components would negatively impact beneficial bugs) if they were released into the environment. Industry assurance and USDA-APHIS general acceptance that microorganisms do not pose a hazard to human health, whether they occur naturally within the plant or are placed there through r-DNA techniques, became a type of security/safety assurance upon which future regulatory decisions were, in part, based. Assessing how pesticides potentially contribute to bacterial growth that is hazardous to plants, however, was not explicitly within the authority of the USDA's role in the Coordinated Framework.

With the implementation of the EPA, the U.S. government took active steps to protect the public against future health and environmental hazards by enabling the new agency to assess and regulate industry chemical products—which required an increased dependency on scientifically supported evidence of safety. From the start, the EPA was established within the context of conflict between competing social and economic divergent interests. In order to "sustain a well-articulated attack" Nixon's Advisory Council gave the EPA the responsibility to not only establish standards that effectively

protected public and environmental health but also the authority to enforce those standards. But in establishing EPA parameters of the level of safety required for regulating pesticides, FIFRA Act qualified the phrase “unreasonable risk”, which could be perceived as subjective and prone to divergent perceptions and is a key area of conflict in determining what is considered necessary to protect public and environmental health and what is considered necessary in promoting economic progress.

By the 1970’s, U.S. legislators were wrestling with a new paradigm of thinking that challenged the boundaries of basic assumptions about growing food and food safety. There are two significant pieces of legislation that illustrate how science, technology and industry became priority factors in further advancing national goals, The National Science and Technology Policy Organization and Priorities Act of 1976 and the Stevenson Wydler Technology Innovation Act of 1980. With the introduction of these two acts, innovation, from the perspective of U.S. legislation, is used in conjunction with technology and industry. For agriculture, the perspective that biotechnology was the next phase of agricultural evolution highlighted the potential for humans to improve the world around them through innovation. But from a critical theory perspective, these two Acts began, in an official capacity, to transition the innovation of the U.S. agriculture system from a civil society endeavor to a corporate industry endeavor that diminished the role and influence of the public (and increased the role of capital-strong business) in how the U.S. food supply was grown. Perhaps it was assumed that if appropriate criteria were met that the science would speak for itself. With the Bayh-Dole Act and the Stevenson-Wydler Technology Innovation Act of 1980, the U.S. government has attempted to stake

a claim in bio-agricultural technology development as a means to secure rights to use products in exchange for federal funding through technology transfer agreements. The academic point of access, however, is limited not only to the extent that academic innovation applies to national and geo-political goals, but also in the influential role that industry maintains with legal rights to intellectual property and patents. This role allows industry to direct the scope, focus and how/whether the outcomes are disseminated, which, in turn, limits scientific exploration and knowledge development and thus constructs domains of perceived safety by maintaining a more predictable body of "available" evidence. Reflecting on Payne and Samhat (2004) when they stated that "[o]ur knowledge of material "facts," for example, cannot be disconnected from the social understandings or interpretations of those facts…" (p. 14). One can see that social construction and critical theory apply in how this new knowledge system enables industry to establish boundaries of knowledge development for not only public and independent researchers but also the public.

As an advocate for environmental protection, the systemic impact of the EPA's decisions could create economic barriers for other federal departments and/or commercial industries, which puts the EPA in a difficult and sometimes unpopular position of regulating politically and economically significant components of industry. To the EPA's credit, they have developed a comprehensive set of criteria that is meant to address the systemic impact that glyphosate might have on the environment or public health. (To the registrant's/petitioner's (Monsanto's) credit, the studies that Monsanto submitted met most of the EPA public health and environmental impact data requirements, assuming the

studies were conducted and interpreted with competence and integrity.) Set in the context of the enormous task that only makes up part of the EPA's total obligation, it seems that the EPA was trying to do what it could with what it had at the time and making the best of it. Without having to produce the data, the EPA could then focus on evaluating the data and setting standards. In addition to assisting the EPA with obtaining the necessary data in a timelier and less costly manner (in terms of federal spending), requiring industry to provide the safety data provided the necessary validation to produce an abundance of data that supported their products. When the GAO reviewed the EPA in 1986, and suggested they use industry-led studies to help alleviate the work load and expedite the assessment process, the lack of discussion, in this review, regarding conflict of interest suggests a high level of trust that industry registrants would provide unbiased data. Since U.S. public food policy relies on science-based risk assessment, it is critical that the standards for validating, assessing and using scientific knowledge are unbiased. Working with industry stakeholders helped to meet the needs of commercial interests and helped relieve government agencies of the time and resources necessary to conduct safety studies.

The Economic Research Service of the USDA's statement that, "[a]gricultural biotechnology is rewriting the rules in several key areas—agricultural policy, industry structure, production and marketing, consumer preference, and world food demand—and public policy is struggling to keep up" could simply be taken as a message that the innovations of agricultural biotechnology were developing quickly and utilizing or changing the existing infrastructure to meet its needs, or, the perceived needs of the

global food supply, and government agencies were not leading this initiative. Add to this statement: “Critical to the efficient and equitable advance of agricultural biotechnology is determining the unique role of public research and when and how the public sector should interact with the private sector”, in addition to CBI agreements and the OMB “Guidelines” and the tone shifts from surface-level free-market capitalism to the underlying roles of public researchers, industry, government and the public (USDA, Office of Communications, Mar. 2003, p. 8). Add the experiences of former USDA researchers, Dr. Kremer and Dr. Lucero, and the tone shifts further, providing an example of not only how public research is playing, or not playing, a role in the public’s (informed) capacity to interact with the private sector, but also how agency information is prioritized to protect major policy decisions and industry interests.

To reiterate Diamond and McDonald’s (1996) analysis of multi-track diplomacy, “[p]eoples, cultures, religious, ethnic or political identity groups, and private citizens have no formal standing in the present global system” (p. 26). This could also be extended to the influence of independent scientists and researchers when their work does not support the current geo-economic system. In addition to the indications (implied or directly stated) that some research is considered unnecessary or invalid, researchers have expressed that there is a distinct separation between their work and the capacity to influence how it is perceived, translated and applied in the making of public policy and regulatory standards. Knowledge development, in this sense, is compartmentalized—scientists produce and interpret specific outcomes within the context of a specific study (e.g. data and analysis from a toxicity study) and policymakers further interpret and

generalize those outcomes to apply within a broader, societal context. It seems there is a valuable resource that is neglected if scientists who know the subject, data and interpretations (e.g. Kremer, Lucero, and particularly Huber, who is a researcher as well as a member of a federal committee that is expected to contribute scientific input that could influence public policy) are not further involved in helping to develop appropriate generalizations and societal applications.

Clarifying agency roles became a central issue as agencies struggled to determine how agricultural biotechnology fit in with the existing standards and whether there needed to be new regulations established to ensure public and environmental health. With the introduction and promotion of agricultural biotechnology, the federal government had an obligation to develop an appropriate system of oversight. Coordinating and regulating a new science and technology—especially one so controversial—within and between a multitude of government agencies, departments, administrations and committees proved to be quite challenging. Overseeing the Coordinated Framework for Regulation of Biotechnology, the OSTP (June 26, 1986) operated from a position that regulation needed to be flexible in order to address potential risks associated with biotechnology (particularly related to food and agriculture) as those risks became better understood. In the attempt to promote further research into the potential impact of transgenic crops, the EPA's proposal to evaluate transgenic crops (under the Toxic Substances Control Act) suggested that transgenic crops were not substantially equivalent. The subsequent rejection of that proposal is suggestive that the flexibility necessary to adjust regulations

according to newly developed science or scientific discoveries, would be limited to the extent of product, rather than process.

Without an intervening step from seed development to field trial, the USDA - APHIS was able to pattern genetically engineered crop regulation in accordance to their pre-existing regulatory authority over conventional crops—in terms of plant protection. By the time Monsanto petitioned AHIS for NK603's non-regulated status, APHIS' role focused on the environmental impact of how plants would interact (particularly if they would alter the DNA of non-target plants and become a containment threat or if the bacterial and/or viral transgene components would negatively impact beneficial bugs) if they were released into the environment. Industry assurance and USDA-APHIS general acceptance that microorganisms do not pose a hazard to human health, whether they occur naturally within the plant or are placed there through r-DNA techniques, became a type of security/safety assurance upon which future regulatory decisions were, in part, based. Overall, although the USDA has played a key role in enabling the prolific growth and expansion of genetically engineered crops, including NK603. The development of federal policies that inhibit "process-oriented" regulation positioned the USDA in a fairly insignificant role in terms of assessing and regulating genetically engineered crops for toxicological impact on humans, animals and even plants.

Federal assumptions of a flexible system that would allow regulatory changes as science evolved and new knowledge surfaces is limited to the sources of science from which the new knowledge derives. The flexibility required to regulate from a "we'll cross that bridge when we come to it" stance works to protect the public only when the risks

for the public are appropriately and thoroughly explored and assessed. Such flexibility requires integrating a multitude of stakeholder voices and expertise, otherwise the bridge disappears in the absence of, or neglected, observation of available data.

Defining Roles in the E.U.

Although the regulatory legislation for Roundup formulations still adheres to a separation of the active from inert ingredients, the E.U., unlike the U.S., recently amended glyphosate regulation by explicitly banning the inert ingredient, POE tallowamine, from being used in conjunction with glyphosate. What this illustrates is that although harmonizing standards (discussed below) enabled transboundary integration of transgenic crops and agricultural chemicals, setting those standards in writing, did not necessarily mean that all parties agreed on them to the same extent. In terms of risk assessment, the E.U. has developed a more extensive regulatory approval process than the U.S., which involves approving GMO products on a case-by-case basis. There is a distinct contrast in the approval process and level of active political acceptance of GMO's between the E.U. and that of the U.S. For example, where the U.S. assumed that substantial equivalence meant that transgenic crops did not require further toxicity research, the E.U. did not hold the same position, thus requiring Monsanto to submit toxicity studies with their application for E.U. NK603 approval.

In creating government regulations, whether it's to help meet the needs of community, protect the interests of a nation or streamline interactions between a community of nations, amendments to previous legislations illustrates how politics strive to encompass and regulate the web of social-political-economic scenarios. Legislative

action to resolve evolving and/or new problems lends to a perpetual growth to the volume and complexity of the regulatory framework as new contexts (e.g. shifts in societal interests, needs, values, etc.) arise that require new, or amendments to existing, regulation.

Harmonizing Glyphosate

The E.U.'s regulation EC 1272/2008, as a whole, is an attempt to address the needs of societal health while optimizing local to global market opportunities through trade continuity. The provision to accommodate third country regulatory requirements grants permission to E.U. decision-makers to use existing data and to over-ride alternative data sets if they are based on criteria that is divergent from the third country standard (in this case, it would be the U.S. standard of assessing only the active ingredient). Amending EC 1272/2008 with EC 1907/2006 by removing the provision for developing "alternative methods for the assessment of hazards of substances" makes the 2008 version cohere more effectively to the trade continuity objectives on which E.U., U.S. OECD and WTO regulatory decisions are based. What this means for the glyphosate safety assessments that help shape policy and regulation in the U.S. and European Union is a continued adherence to industry-led research design that promotes a narrowly defined (as opposed to holistic) analysis that has been demonstrated to produce industry-favored outcomes.

Harmonizing NK603 (GMO's)

Integrating federal initiatives with industry-led research promoted harmonization in terms of boundaries of validity for research, development and marketing. In terms of

societal structure, government and government organizations (i.e. OECD) are considered "voices of authority". When those voices of authority determined that r-DNA technology and the resulting products were patentable and subject to private legal rights, such knowledge and technology became the privilege of those who controlled the rights. In addition, when the voices of authority determined that agricultural biotechnology was substantially equivalent to its conventional counterparts (as long as the transferred gene was considered safe), the resulting messages of GMO safety and significant integration into the U.S. (and global) food system could be viewed, from a social construction perspective, as actions that contribute to mainstreaming societal perceptions of product acceptance (i.e. "normalizing" the product) by limiting official recognition of conflicting evidence. Socially constructing a product as "normal" could contribute to a more compliant society in terms of accepting new technologies. However, as new conflicting science emerges (and society is exposed to new realities via unofficial venues) despite these normalizing efforts, we begin to see disharmony through increasing societal resistance (particularly in E.U. where societal resistance seems to influence government action) in regards to the established standards. On a similar note, as with harmonizing glyphosate, collaborating with multiple stakeholders to develop standard toxicity test criteria that multiple parties agreed upon promoted a level of shared assumption that if those standards were followed there would be a higher level of safety in developing and marketing products approved when they met those standards (and the results met with established criteria for safe human consumption). As was indicated by E.U.'s recent ban on POEAs, however, it is clear that the standards for safety need to be revised. If we look

at harmonization from a critical theory perspective, societies are challenged between promoting standards that define "sound science" (and, therefore, standards for safety) and promoting exploration that could further develop our understanding of the barriers and benefits of our constructed realities. Let me reiterate a quote from chapter one that states that technical rationality "on the one hand…was a critical arbiter and espoused the ideal of impartial analysis of truth and on the other hand it became the instrument of perpetrating domination of nature and humans by technicalising administrative, political, and bureaucratic processes" (http://www.unipune.ac.in/snc/cssh/ipq/english/IPQ/21-25%20volumes/25%2002/PDF/25-2-7.pdf).

Theme 2: Data Access Restrictions

The Bayh-Dole Act shifted the perspective of knowledge as a shared public domain to one of privatized limited access. It allows academia (and other private and public organizations, corporations and institutions) the capacity to capitalize on specific research outcomes. In a sense, academic knowledge becomes a commodity in a system that compels universities to compete with industry. But, in shifting the purpose and motivation of academic exploration and discovery, is there an implicit concern regarding the potential impact that economic incentive and patent protection/barriers could have on the integrity, creative exploration and potential breadth and depth of research?

Beginning in the 1980's, the flourish of agricultural biotechnology development, along with the Bayh-Dole Act, offered a potential new reward system for academic researchers (and the institutions for which they worked) that included not only the potential for professional accolades and peer recognition for advancing innovative

technologies that were valued by the federal government, but also the potential financial payoff that patenting knowledge processes or innovations could potentially generate from products valued by the commercial market. In other words, there is quite a bit of potential in discovering, developing and marketing a product, but generating the public funds to realize that potential proved to be a challenge that many universities could not overcome.

Public and independent researchers found themselves not only financially challenged in funding new research, but in terms of studying existing products (e.g. components in Roundup), key ingredients and formula recipes are legally made inaccessible to those who do not own the patent rights. Financial and information privileges could be viewed in terms of critical theory in which those who have the financial capacity quite often are the ones who control the information, particularly in terms of biotechnology development. Recall Congressional discussions in the 1970's that transitioned biotechnology research from a public to private endeavor (because the U.S. government could not sustain the financial burden of such research) and Miller's statement regarding how, since the 1970's, the biotechnology industry dictated federal agency decisions and actions. The Regulatory agencies, such as the EPA may have access to such information in order to assess product safety, however, all but the active ingredient is often censored when disseminated to the public (e.g. product labels and agency memorandums), making independent research quite challenging. Recall the EPA memo stating that two inert ingredients were exempted from required tolerance levels. The identity of those two inert ingredients was blacked out, presumably for proprietary reasons. Without public accessibility to the identity of those two inert ingredients, the

possibility exists that one of those ingredients was POEA or a version of it. Intellectual property rights make verification difficult, which, in turn potentially casts doubt on the EPA's long-standing assumption that all inert ingredients with unregulated status have been proven safe.

Protecting Innovation: Benefits and Barriers

Intellectual property rights and the patent system have been critical factors in shaping and developing how agricultural biotechnological data is created and who creates it. Recall that when the Supreme Court was deliberating over whether to permit Chakrabarty to patent his lab-created bacteria, former Justices Brennan, White, Marshall and Powell raised concern regarding monopolizing life forms. Not only was their concern never directly addressed in that case, but since then the U.S. has slackened anti-trust laws, enabling biotech industries to further secure these rights by consolidating seed production. Considering the cost and time it already takes to develop bio-agricultural products and secure them within an increasing field of overlapping patents, streamlining biotechnological product development by collaborating with the competition makes prudent financial sense. But there remains the question of whether consolidation, on the other hand, stifles innovation by restricting innovative diversity. This is where independent and publicly supported research (of which the majority of biotechnology was in the 1970's) enables, rather than inhibits, exploratory discussion because the research is set in the context of public ownership rather than protected proprietary domain and the goals are towards developing for public benefit rather than private security.

As the numbers of patents increase, however, transparency decreases as a protective measure against competition. Overall, in the U.S., a decrease in public R&D and increase in private R&D for what is promoted as a critical source of multiple forms of national security shifts knowledge generation and dissemination from publicly accessible data to privatized data that is protected by intellectual property laws and patent rules. In other words, the safety and viability of a key tool used to help secure major U.S. interests became significantly dependent upon private sector knowledge.

In an effort to alleviate some of the imbalance caused by company control over intellectual property, the Bayh-Dole Act of 1980 was enacted, but the Act does not address the need to increase public research access to existing industry data/property. Although Monsanto, with its statement regarding increasing researcher access to their products "with as few constraints as possible" is meant to show good faith efforts at transparency, the qualifying term "as few…as possible" leaves room for debate regarding access, research design, outcome interpretation and dissemination. This debate was evidenced in Pollack's (Feb. 19, 2009) article, suggesting that academic or extension researchers who want to study current biotech products independent of the industry who owns it/them have been inhibited—not only potentially from sharing the information they have gleaned, but also from accessing the research material in the first place because it is proprietary and subject, mainly, to the rules of the company that owns the product. Barriers were not limited to academic and extension researchers, in addition, the 26 scientists, who were pulled together to work on a project for the USDA and EPA, that complained about the explicit research limitations of technology and stewardship

agreements suggests that even government sponsored can be restricted by intellectual property rights. What this indicates is not only a potential for unchecked hazards, but also an opportunity for both the USDA and the EPA to improve transparency policies between industry and public researchers by further developing and utilizing policies that support research integrity and scientific rigor from the scientists hired to conduct research on behalf of the federal government. Limiting the capacity for independent or publicly sponsored researchers to access primary research material limits the capacity to create an informed public. Although Monsanto's response is encouraging, the legal authority of intellectual property rights, while understandable from an industry perspective (e.g. protecting one's investment), could technically maintain the right to limit research and potential critical discoveries important to public and environmental health.

From a patent perspective, the root of it is economics—creating the necessary safety and efficacy data for a single biotech product can take over a decade and require an enormous amount of financial and expert input. As noted in the timeline for agricultural biotechnology product development since the 1980's, competition in the commercial setting means that timing is critical in researching innovative products and shared information can be detrimental to future patent security and financial profit. Allowing industry more leeway to conduct, and protect the rights to, research alleviates much of that cost from the U.S. government and, in political terms, promotes a win-win situation in which industry gets financial reward and the U.S. government progresses towards its goal of securing perceived national interests.

While the statements that Monsanto (and other industry interests) make regarding the beneficial role that patents play in providing financial incentive for innovation are convincing, to an extent, what becomes factored into and enmeshed with innovation is an economic component that has the potential to gain priority and/or redefine the purpose of the innovation. Assuring ownership of one's innovative discovery offers patent holders a limited time to balance the books and potentially make a profit. It makes sense, from an economic perspective. However, within this system, knowledge generation becomes a closed-system with limited input from external sources. Framed in this way, Plato's "necessity is the mother of invention" suggests that initial motivation to invent might be to fill a societal need that could be satisfied by the invention but, to a certain extent, motivation inevitably transforms into a personal financial need satisfied with secure private ownership and rights to the solution. Along with this transformation arises the potential for tension between society and inventor when societal needs change and make previous innovation less viable.

With the increased production and dependency on agricultural biotechnology, scientists within U.S. federal research programs have stated that they have experienced a more restricted environment in which federal goals for scientific advancement seem to align more with maintaining the integrity of the current (industry supportive) system than accepting and confronting the potential risks involved with exploring beyond current assumptions of glyphosate and transgenic crop safety. This is a strong statement that needs careful consideration because it implies a level of irresponsibility that is not limited to one agency, department, authority or administration. Huber's long-term membership

with the USDA-APS National Threat Pathogens precludes a certain responsibility to share preliminary information if such information has the potential to avert or mitigate a national disaster or serious health risk related to the program mission. The USDA's response, or rather lack of response, potentially suggests that the federal government does not consider Huber's data as evidence of potential crisis, or at least not a significant potential as to risk a major source of financial and political security—but how was Huber's data weighed, in terms of validity?

Kremer's statement regarding the USDA's cautious attitude (regarding what information its researchers were disseminating to the public) could be viewed as striving to maintain accuracy in how data is translated; but requiring that its scientists refrain from sharing their research until it has been "approved and published" eliminates public discussion and potential exchange of ideas regarding current, in-progress research. This policy essentially shields the public from current projects until they are complete. Transparency, through this lens, is available as an end product—the process is not the business of the public. Similarly, the EFSA's (2015) "Conclusion on Peer Review of the Pesticide Risk Assessment of the Active Substance Glyphosate", suggests an apparent distinction between publicly accessible peer review and government peer review.

According to the Office of Management and Budget's (2002) "Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies", the balance of transparency extends only as far as confidentiality agreements allow, necessarily limiting public access in favor of industry protection. CBI effectively veils a company's secret formula and protects their

investment from competition, thus following the logic of patenting and promoting intellectual property rights. But from an independent scientist or consumer perspective, veiling certain ingredients as CBI makes it difficult to compare specific products with active ingredient studies verses studies with surfactants and studies that analyze both active ingredients along with specific surfactants. But if Newton's "shoulders of giants"—the cumulative knowledge and experiences of our predecessors—are veiled or inaccessible to those outside of the dominant bio-ag-tech innovation circle, a large pool of independent innovators is operating from a disadvantaged position that also, in turn, limits timely independent input into the biotech knowledge production system from which policymakers gather their policy-supporting data.

Transitions: Public to Private Research

It became clear with the implementation of the Act that although the federal government still recognized the value of public knowledge creation, industry was given a leading role in advancing and securing national priorities such as agricultural production. Reflecting on Diamond and McDonald's (1996) analysis, the consequence of such geo-economics is an increasing protective barrier between public policy and public influence. From the Committee for Scientific and Technological Policy meeting in 1983, one can see a national transition from public to private research and development designed to bridge academia, government and industry.

In order to bridge public and private needs and interests, the EPA (and to a lesser extent, the FDA and USDA) has striven to obtain a holistic understanding of how a product will impact society by requiring a wide array of pre-market data (on certain

ingredients) demonstrating product safety. Requiring such additional research can be quite expensive and to alleviate some of the costs the federal government offers grant opportunities to private and public agricultural R&D efforts as a means to promote food security, generate economic growth and increase competitive advantage in the global market. The regulatory trends for bio-agriculture have focused on promoting a national agenda by streamlining a particular type of innovation that, economically speaking, seemed more feasible to advance as a private commodity than a public endeavor. Providing such support, the government, in addition to private (and public) entities can often have a significant amount of time and financial commitment into a singular product or process (which can make criticism and change difficult to accept when one is so deeply invested).

Unpublished Data

Agricultural biotechnology policy development within the U.S. and the E.U. has depended, in large part, on the data and safety assessments of unpublished industry studies. This means that the raw data was not publicly accessible, therefore making the assessment process non-transparent, thus also making a significant part of policy development non-transparent. Public participation was limited to second hand discussions about the studies and their subsequent assessments. The study conducted by IARC challenged assumptions of validity by specifically using publicly accessible research, which subsequently omitted the use of the unpublished industry studies upon which current U.S. regulations for glyphosate/Roundup are mainly based. Reflecting on Kremer, Huber and Lucero's research and the evidence of increasing public and the independent

studies described in Domingo and Bordonaba's (Feb. 5, 2011) literature review, it has become evident that since 1994, the number of independent, integrated and long-term studies has increased, lending to a more comprehensive knowledge base on glyphosate and transgenic crops that is not reflected in U.S. federal regulation. IARC, in utilizing this expanded knowledge base, is promoting the continuation of scientific discovery, highlighting where the system is flawed as a potential tool to help correct the criteria of what is considered valid input and potentially improve the quality of the output, and thus potentially advance the integrity of the system as a whole.

General Barriers

Trying to access government peer reviewed studies proved to be challenging. The EPA's Tier One assessment report had listed several studies that were not found on the EPA's website. If it was submitted to the EPA, it is reasonable to expect, at minimum, a reference citation detailing who submitted the study, what the title/purpose of the study was and when it was submitted. A significant level of transparency is lost when the supporting evidence is not accessible for public review. Another barrier I experienced in my research was in trying to access government information on the recent German (BfR) glyphosate report. Although broken links are not uncommon with online material the consistency of dead-ends for links that I experienced in trying to find information regarding the BfR report has challenged my trust regarding the EFSA's commitment to promoting transparency. This contrasts with IARC's report, which is easily accessible and demonstrates effective transparency by listing its authors and their professional affiliations as well as including in their assessment only publicly accessible and valid

(peer reviewed) data. Even the BfR's use of "so-called 'peer review procedure'" suggests a potential discrepancy in perceived scientific rigor between the BfR and standardized E.U. procedure. The peer reviewers' identities are not explicitly stated in either the BfR or the EFSA summaries, therefore, it is not clear how the experts are related to the subject of study (e.g. field of expertise, conflicts of interest) what their criteria was on which their conclusions were based. Without knowing who conducted the review, a significant level of transparency is lost.

Theme 3: Data Gaps

Regulating only the active ingredient (glyphosate) meant that pesticide residue testing was conducted on only the active ingredient. Between the USDA's Pesticide Data Program and the FDA's Total Diet Study, one might assume that (considering glyphosate is one of the leading pesticides used in the world) foods derived from glyphosate-tolerant crops would be checked periodically. However, since glyphosate was categorized as lacking evidence of carcinogenicity the Agencies have not considered it a priority pesticide to test. But there is growing evidence to support early warnings that the data selection process of the current regulatory system is contributing to hazardous data gaps, particularly if one considers the FDA's statement that it was weighing the cost of implementing glyphosate testing with the "extent of the use of genetically engineered crops for human foods". However, the last complete RED for glyphosate (in 1993) was determined without exposure assessment data from the PDP. The FDA is also responsible, in part, for monitoring pesticide residues to ensure that tolerance levels are not exceeded on food. But in regards to testing glyphosate, the FDA's statement that they

were weighing the costs and benefits in terms the "extent of the use of genetically engineered crops for human foods", does not explicitly include conventional crops that use glyphosate as a growth regulator. In addition, the strength of the USDA's claim that its pesticide residue testing program is "the most comprehensive…database in the U.S." diminishes if one considers that a leading agricultural commodity (corn) essentially has not been analyzed for the herbicide most commonly used on that commodity. Since 1993, the EPA, FDA and USDA have rarely tested for glyphosate residue, which, in turn, means that NK603 and glyphosate and its formulations have largely been used without federal oversight. E.U. resistance to GMO integration continues with reference to the gaps in the currently accepted scientific data, which suggests that the evidence of safety is not conclusive.

The EPA, policy makers and industry also claimed that glyphosate is a non-endocrine disruptor. But the commercial variations of Roundup do not only contain glyphosate, but inert ingredients as well—POEA's being one of them. While the EPA's most recent assessment of glyphosate emphasizes the need for more data on glyphosate formulations, based on the EPA's "uncertainty about its risk to aquatic animals" (EPA, June 17, 2009), the absence of explicit reference to the need for toxicity research that demonstrates safety in terms of human health is a point of concern. It also highlights a gap in the EPA's four-part integrated risk assessment created by testing only the active ingredient when the formulation is known to be more toxic. But the independent studies that the EPA reviewed and conducted, and which concluded that glyphosate formulations were toxic in several contexts could have been perceived as evidence simply that the

adjuvants were more toxic than the active ingredient and thus did not change the EPA's recent re-registration of glyphosate. Requesting more data on POEAs and glyphosate formulations is a step towards a better understanding how the parts work as a whole (if the data they assess opens the system to available alternatives to currently assumed outcomes). But without incorporating a comprehensive data set that opens assessment to alternatives to the previously accepted studies, conclusions of safety seem premature and unfounded.

Séralini was the first to conduct a toxicity study NK603 (ten years after it was approved by the USDA) that was longer than 90 days for chronic toxicity and one of the few to study the toxicity of glyphosate formulations in a rodent study (there were already several aquatic fish and amphibian tests that concluded glyphosate formulations were toxic). In recognizing gaps in what an acute and 90-day toxicity studies and active-ingredient-only studies can provide regarding long-term health effects, Séralini was advancing one of the goals of scientific inquiry and experimentation by conducting research to try to fill in those gaps. On the surface, it appears that part of what is driving this conflict is a divergence in how the results of these studies are interpreted, but underlying this seems to be conflicting perceptions of the existence of a gap.

The 1982 OECD report noted that there needed to be a concerted effort to better understand basic plant science if agricultural biotechnology prospects were to be realized. The EPA's 1984 proposal that microbial research might demonstrate new substances derived from r-DNA manipulation seemed to mesh with the OECD suggestion, but the U.S. OSTP denial of the EPA's proposal and subsequent establishment of standards of

equivalence diminished the perception that we had more to learn on the subject. By 1986, the OECD had determined that concerns about unexpected pathogens and infectious diseases were unfounded based on the scientific evidence at the time which resulted in relaxing regulatory standards.

Just recently, however, the National Academies of Sciences, Engineering and Medicine (2016) recognized a general need to further develop our scientific capacity to identify and address unintended changes resulting from GE and conventional crops but they emphasized “new crop varieties”, thus, essentially implying that existing crop varieties were exempt from further study. This is another point of concern, considering that, according to researchers such as Kremer and Huber, we currently haven’t fully developed the capacity to effectively and conclusively identify the extent to which unintended changes occur or appropriately address these unintended changes within the regulatory system. It seems that the stated intentions to maintain a flexible U.S. regulatory system, capable of adapting to newly identified risks, has become rigid and inhibitory of change in regards to existing products. If one reflects on Week’s (1994) precautionary statement regarding the potential consequences of a nation relying on the success of a limited number major exports, and include that this success is supported by a limited set of research standards and outcomes, U.S. national security has become dependent upon what appears to be increasingly inadequate science.

Theme 4: Perceptions of Safety and Validity

Transitions: Basic to Applied Research

U.S. policy specifically suggested that toxicity studies were not required because of the assurance that gene transfer techniques were not only precise, predictable and safe but also resulted in an end product virtually the same as its parent.

As the emphasis of innovation shifted from meeting specific societal needs to maintaining viable economic (and political) outlets (as evidenced in the language of the Stevenson Wydler Technology Innovation Act and the National Science and Technology Policy Organization and Priorities Act), the economic success of the innovation depends on the capacity of innovator and innovated product to evolve (or at least be perceived to evolve) with needs of society. In order to meet evolving crop protection needs and maintain market viability (some of which were largely created from the initial innovation, e.g. the increase in glyphosate-resistant weeds) bio-tech seed developers might evolve a product, i.e. change their pesticide formulations. Conversely, as a patent right expires, bio-tech seed developers, as in the case of Monsanto and NK603 (transitioning from Roundup Ready I to Roundup Ready II) might illustrate the transition from meeting societal needs to innovating in order to meet individual economic needs, although the new product includes new attributes that are marketed as desirable—they do not necessarily fill a need. Underlying this discussion is the issue of innovation that is needed to address problems created by previous innovation. From this perspective, the quality of innovation is diminished if, in time it creates a new societal problem or exacerbates an existing one. Innovation motivated by investment does not necessarily factor in societal

need as much as it factors in the perception of need that will likely be necessary to effectively market the product. Applied knowledge refocuses scientific exploration to a narrower problem-solution orientation and R&D moves that exploration into development of specific products. R&D is a valued contribution to the U.S. economy that produces bountiful innovations for our society, but it is important to remember the limitations of applied research and R&D when the goal is toward a specific (potential) commodity.

Kahan's, et al (2013) study provides an example of how social construction operates to shape our realities. There is an underlying question regarding the cultural influence on the scientists themselves in how they interpret and present their research. For example, as part of an ethical practice in transparency, researchers are encouraged to state their biases and potential conflicts of interests as a means of not only qualifying their personal frames of reference, but also as a starting point in recognizing and, to a degree, validating, opposing or alternative perspectives. But when academic scientists are funded by, or have professional ties to, private interests, there are often underlying commitments and expectations between funders and grant recipients. When grant recipients do not openly admit those affiliations (and the potential risks inherent) and offer personal strategies to counter those risks, then, as Kahan's study suggests, it is not unreasonable to ask whether membership, recognition and validation within the private funder's culture motivates scientists to select and interpret data to better meet the needs of the funder. While academic researchers, scientists and government employees who volunteer their time on an industry board or are hired by industry interests does not

automatically assume that their research is invalid or that their ethical standards have been compromised, it does, however, leave an opportunity open for conflict of interest to develop if one considers the power of social construction in developing us v them, insider/outsider perspectives that influence the boundaries of worldviews. In less theoretical terms, a window of opportunity arises if the researcher's employment (financial) and/or professional status is suddenly elevated or placed at risk if their work meets or contradicts the goals of the industry within which they work. With this in mind, even if a researcher, employed or otherwise associated with a certain party, maintains ethical standards in which his/her work is conducted with scientific integrity and rigor, and presents that work in the context of a party that has a financially vested interest in the outcome, they could still face perceived bias from a party negatively impacted by those outcomes.

Since the 1970's when the future of agricultural biotechnology was first tentatively envisioned throughout the Asilomar conference, to today, independent scientists have expressed concern regarding how biotechnology science and the knowledge stemming from it might be used in the context of public protection, public education, and commercial application. Government has expressed this concern as well, as detailed in the OMB's Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies; but is the context the same? The implementation and permeation of intellectual property rights has shifted the context from the open dialogue of the Asilomar conference to protective censoring. Berg (Sept. 18, 2008) suggested that, for this reason, another

Asilomar Conference is not foreseeable, however, in the spirit of transparency, such a conference between (former) public and independent researchers might still be possible in terms of discussing national goals, "alternative" research and how to integrate relevant, but currently unused research into the agricultural system (see Recommendations for further discussion).

Weight of Evidence

It seems that some of the current research that can begin to fill the gaps discussed in Theme 3: Data Gaps is being systematically rejected, perhaps through the flexible use of "weight of evidence". Weight of evidence has been used, for example, within the EPA, the EFSA, and the FAO/WHO JMPR reports, but as discussed, there is not an established criteria regarding what research is included, which thus implies that the criteria for determining the data sets (i.e. the knowledge basis) for safety assessments is not necessarily harmonized within and between agencies, health organizations and policymakers. It might seem prudent to establish a clear definition of an approach that is used to help health officials and policy makers determine safety parameters in order to understand how/if the contributions of scientists like Huber, Kremer and Lucero are "weighed" into the assessment process. Considering the research of Balls, et al (Dec. 2005) and the OECD (Apr. 13, 2012) statements, the criteria for determining the data sets (i.e. the knowledge basis) for safety assessments is not necessarily harmonized within and between agencies, health organizations and policymakers. But considering Sowell's (2007) note, there needs to be a flexible component, within the harmonization process, that allows for contradictory evidence to be recognized, validated and appropriately

utilized within the standards of Science, rather than scientific standards developed for the sake of streamlining commercial development and trade. In other words, what seems to be lacking in the current geo-political system is acknowledgement and understanding of the benefits and consequences of public policy that is shaped and supported by Science and science that is shaped and supported by public policy.

Considering the lessons learned from restrictions and bans stemming from the PCB industries' inability to prove safety (of which Monsanto was a part), it makes sense that the agricultural biotechnology industry would ensure, scientifically, that their product was safe (but this is based upon my own speculations of unarticulated cause and effect). Developing an extensive base of supporting scientific data provides more than a means to justify one's claims, it also provides one a basis to deny the validity of research that challenges those claims. Industry had supplied the majority of the studies on glyphosate and genetically modified crops (recall Portier's et al, (Mar. 3, 2016) comparative analysis between IARC's and the EFSA's glyphosate assessments) and the evidence considered in recent policy-making remained weighted in favor of industry. Thus, by producing enough supporting (and government-validated) data, regulatory policies could be influenced in one's favor.

Parts vs Whole: CP4 Enzyme and NK603

Similar to the EPA's decision to separate the formulated components of pesticides into regulated (active ingredient) and non-regulated (inert ingredients) components, the FDA and USDA separated the transgenic process (non-regulated) from the transgenic product (regulated). Genetically engineered food is regulated the same as conventionally

grown foods as long as there is data to demonstrate that the parts (the transferred DNA) do not pose a hazard and the end product is shown to be “substantially equivalent to its conventional counterpart”, thus suggesting that no further research was necessary.

Although the U.S. and the OECD claimed substantial equivalence, the product verses process is useful in describing key differences between U.S. risk-based policy that promotes regulatory decision-making in terms of end-product attributes and E.U. precautionary policy that promotes decision-making based on not only how the process impacts the attributes of the end product, but also its potential impact on a broader socio-cultural level.

Parts vs Whole: Glyphosate, Inerts, Roundup

The EPA, under increasing pressure from the GAO to make their safety assessment process more efficient as the number of chemicals entering the market increasingly outpaced the number of chemicals assessed, separated and independently assessed the components of pesticides as active ingredients and inert. The EPA’s system of breaking the formulation into components seems to contradict the goals for a whole-systems integrated approach. Although the EPA had set tolerance levels for glyphosate, many adjuvants, such as POEA, were exempted from standard tolerance level/regulatory requirements, which suggests that those adjuvants are non-toxic. This enabled the EPA to establish a base of ingredients that, if they meet safety criteria, did not need to be regulated (and thus, did not have to be tested with each new registration or re-registration). From this perspective, it follows that testing glyphosate pesticide formulations might be considered unnecessary if the adjuvants used have already been

approved for non-regulated use. The shift from the EPA's 1995 determination that POEA be categorized in List 4b--current use pattern…will not adversely affect public health and the environment, back to List 3 (unknown toxicity) for a substance apparently not regulated but commonly used with the world's most prevalent herbicide could initiate concern regarding in its potential to negatively impact public health. But early warnings from researchers such as Folmar, Sanders and Julin (1979) within EPA memos indicate that the EPA was aware of the potential hazard of POEAs and Roundup formulations even prior to the initial glyphosate RED in 1986. Although awareness of the co-formulant hazard would not impact the re-registration of the active ingredient, it calls into question the validity of the EPA chemical assessments in regards to how the other inert ingredients were assessed and the integrity of the system of separating the formulation into parts without assessing the formulation as a whole. Other research followed that supported Folmar, Sander and Julin's research (e.g. McLane, Howe et al, etc.) and further concluded that POEA's not only have carcinogenic potential on their own but that they also exponentially increase the potential carcinogenicity of the active ingredients with which they work.

The BfR's lengthy recommendation that the recent review of IARC's report on glyphosate suggested that the assessment would be more appropriately discussed and resolved between all of the stakeholders rather than through a single RMS. This is a potential indication that perhaps more than science is required to make recommendations or determinations.

Data Details and Interpretations

But a closer look at the studies reveals inconsistencies. For example, it would seem that in an effort to maintain consistency, a rodent study would not be acceptable as support for the requirements of a non-rodent study, and an Acute dermal study would not be accepted as support for a chronic feeding study. Reflecting on the scrutiny with which critics (including policy makers) of Séralini's el al (2012) study analyzed the study's adherence to OECD guidelines, it seems relevant to question why the same scrutiny was not given for the re-registration of glyphosate. Another detail that seems inconsistent involves the glyphosate studies from Monsanto (Hammond, Dudek, Lemen and Nemeth Feb. 12, 2004) that illustrated a significantly higher NOEL in the 90-day study than the 2-year study. Genetically modified crops differ from their companion pesticides in that they are not tested according to NOEL (except for measuring pesticide residue)—they are not tested for toxicity at all in the U.S. In the E.U., a 90-day rat study sufficed for assurance that NK603 was as safe as its conventional counterpart. This is a little like comparing apples to oranges, but there is a nugget of logic that supports the idea that if a chronic test for a chemical could produce such a drastic change in the NOEL, then perhaps it is possible that a chronic test for a novel food could potentially indicate toxicity, especially considering the widespread integration of corn throughout the global food system and the intention of the OECD to replace conventional crops with GE herbicide-resistant crops. Couple that with Kremer and Huber's (among others') research and OECD guidelines that link the length of time required to test a product to (in part) how much the commodity or substance (to be tested) is expected to be produced, it seems relevant to

propose appropriate, comprehensive testing (short and long-term) of transgenic crops as well (EPA, July 2000).

With the EPA's final interpretation of the mouse study (from the 1986 RED for glyphosate) and subsequent determination that glyphosate be assigned as a Group "E" pesticide (strong evidence of non-carcinogenicity) the U.S. government was able to make a declarative shift from possibly carcinogenic to "no evidence of carcinogenicity" which made it possible not only for instant market application but also the capacity to increase application rates to address weed glyphosate-tolerance problems. But the question raised in the 1986 RED regarding the beagle study results that showed changes in the pituitaries, and the 1993 RED description of the study that eliminated any mention of the issue and did not include the requested additional information (from the 1986 RED) that was needed to clarify understanding of those pituitary changes, there is a lingering question of what criteria was used in the panel's final determination and how the gaps in the data were perceived to be filled.

While the EPA had a multitude of safety data on glyphosate, it had passed through two re-registrations (1986 and 1993) without understanding its mode of action. Without a definitive understanding of the mode of action, one is left to guess at how a chemical works—not only within the plant, but also within the surrounding environment and in the human body.

Recall that in a supplemental 13-week study that Monsanto submitted, there were 20 rats/sex/group but only 10 rats/sex/group were analyzed, which is the minimum requirement for subchronic toxicity, according to OECD standards. Since there was no

explanation in the study as to why half of the test subjects were tested, it leaves room for speculation regarding the integrity of such a decision and the validity of the results.

Conflicts of Interest and Public Trust

Ashford's (1984) report regarding industry-weighted data creation *and* assessment could increase the potential for biased reporting in favor of industry products, leading to potential health hazards if certain safety criteria were not met. Such influence in what and how information is created and presented could be viewed in terms of critical theory. This is significant to note for two reasons: 1.) all of the chronic and carcinogenicity studies that the EPA had/has been using for their chronic toxicological assessment and certification of glyphosate (four described in the content and two listed in the reference section) were submitted by Monsanto, and 2.) the EPA determines, for the USDA, which pesticides to analyze in its Pesticide Data Program (PDP) (i.e. with glyphosate designated to List E, glyphosate was not a priority chemical to track). Similarly, the FDA's conclusion regarding the safety of NK603 was based on industry data *and* data interpretation as evidence of NK603's substantial equivalence to its conventional counterpart. Additionally, nutritional equivalency is assumed but not required to be tested in order to obtain regulatory approval for transgenic crops, therefore, the FDA's main responsibility rests with post-production risks to human health.

On the surface, if one simply looks at the interpreted results of the glyphosate studies after the final scientific advisory panel's decision, it follows that the EPA would grant re-registration of glyphosate but it fails to thoroughly address the initial red flags raised by the first two reviews and the underlying potential for biased data and

assessment from sources experiencing a conflict of interest. It is not an excuse for their actions, but it establishes a context for understanding how certain decisions and actions were made, or, not made.

The EC GRACE project and coordinating G-TWYST were implemented as a means to explore translation and communication strategies that could be used to accurately inform the general public about primary data and data interpretations, as well as further investigate whether MON810 (the only GMO maize crop cultivated in the E.U.), the subject in the GRACE study, and NK603 (the subject of the Séralini v Monsanto conflict and the subject of the G-TWYST project) were more hazardous than previously assessed. The Austrian Federal Ministry of Health's response to the GRACE project conclusions invites further discussion regarding how science is conducted and how it is interpreted. I am not qualified to judge the validity of either's claims, but discrepancy regarding the scientific process exists between valid, authoritative parties and this discrepancy is likely representative of a larger issue than just the points raised in the letters between the Minister of Health and GRACE representatives.

Integrative Research

Although glyphosate's capacity to bind tightly to the soil has been a positive marketing point for supporters of glyphosate-tolerant crops who emphasize that this feature limits the occurrence of run-off and subsequent water contamination, since at least the 1990's, public and independent researchers have expressed concern regarding the efficacy of glyphosate hazard assessments in their capacity to address systemic impact on public health. Kremer and Huber are among several researchers who are

discovering unexpected events of transgenic plants and glyphosate (and glyphosate formulations) that negatively impact soil, plant, mammal and potentially human health.

As discussed earlier, the scientific test guidelines of the OECD (Apr. 13, 2012) had been developed and implemented, as international standards for assessing toxicity, through a joint effort between not only its member nations (U.S. and E.U. included) but also industry representatives. Defining the parameters of acceptable evidence of objective proof, the U.S. position on agricultural biotechnology safety is supported by its perception that industry studies, which have demonstrated a certain level of adherence to OECD guidelines, have proven sufficient for U.S. regulatory glyphosate and transgenic crop approvals. However, if certain assumptions about science—assumptions of GRAS, substantial equivalence, or that certain chemicals or biological/microbiological processes behave in predictable ways—preclude the perceived need for additional research, there is a possibility that some scientific research (e.g. Séralini, Huber, Kremer, Lucero, etc.) could be perceived unnecessary or even invalid if it operated outside of the boundaries of the established standards and/or expectations.

When Dr. Kremer's work was reviewed by his colleagues and subsequently dismissed as limited or unsupported in its claim that glyphosate indirectly promotes a toxic pathogen within the soil and plant microbiomes, his response (that the scientists who reviewed his work were "traditionalists"), one might argue that this could simply be a case of a miffed scientist bad-mouthing his critics, Kremer's message warrants serious consideration based on the credibility his research was afforded prior to establishing stronger claims that contradict the standard claims that glyphosate is safe and r-DNA

techniques are predictable. What also warrants discussion is how these perceptions of scientific validity fall in with the concept of scientific revolution.

The push and pull of expanding traditional theory and expounding new ideas can lead to new scientific territory and thus, new discovery, but it can also create resistance and conflicting perceptions of validity from those who adhere to what is familiar. Recall Week's (1994) note about the benefits and consequences of diversity. The benefits being an environment conducive to exploration, discovery and broader, deeper understanding (by inviting a multitude of perspectives and expertise to contribute to the process), and the consequences producing outcomes that potentially take one beyond the boundaries of expectation into unfamiliar, perhaps uncomfortable or difficult realities. The challenge then becomes determining when, and the extent to which, the focus of one's expectations promotes and sustains viable research and when it suppresses the vitality and validity of the scientific process. Séralini, et al's (2012) article was technically valid in terms of established criteria for research article submission; however, the validity of the outcomes was limited to rigid adherence to established standards that promoted a specific set of sound scientific methods that were created as a streamlining aid. Such standards, however, do not preclude the validity of other methods. Such standards simply promote methods that ease verification for mass research, production and trade. Methods that stretch beyond the boundaries of such standards prompt resistance, as indicated by the resistance to Séralini et al's (2012) study, perhaps because they cannot be streamlined and, therefore, require an alternative set of validation standards. Making exceptions to

established “rules” is bound to raise objections and doubt, which in turn illuminate assumptions of what makes for sound science.

What is also interesting is this push and pull within the context agricultural biotechnology, considering the U.S. government’s initiatives to make it the new scientific revolution. If Kremer’s work could be construed as thinking “outside of the box” (e.g. herbicides impacting plant and soil microbiology and the process of transgenic modifications having unintended effects) yet his research was well-designed, appropriately conducted, agency approved and produced consistent results that bring new breadth and depth to our understanding of current agricultural practices, it seems that his work would be invaluable towards advancing national goals of being leaders in scientific revolution. But the reality seems to reflect that the system is stuck between policies and authoritative perceptions that resist such change and verbiage that promotes it.

Lucero’s research could be considered a paradigmatic shift from current scientific trends to something new. This paradigmatic shift could be considered, according to Kuhnian theory, the core of a scientific revolution because it challenges the previously accepted and mainstreamed theory and methodology of how microbes impact soil/plant health within the lab and in the field. Dr. Kremer’s work and the research of Dr. Huber and his colleagues could be considered as pushing the boundaries of paradigmatic shift in that their research challenges current ideologies about the predictability of plant-herbicide interactions (illustrated in the 1986 OECD report) that suggest that scientific studies are not required to investigate or analyze systemic microbial root zone impact. Kremer’s and Huber’s (and colleagues’) research are just two examples that introduce a new level of

scientific development in regards to researching systemic interactions and impact between chemical applications and plant/soil health. Their research could be the beginning of a new level of toxicity identification and health hazard analysis.

Highlighting the experiences of these three scientists is important because for the majority of their careers, their work was federally approved and conducted for the purpose of advancing and protecting the viability of U.S. agriculture. Furthermore, Dr. Huber's positions and memberships within the U.S. government (see Chapter 3 for details) not only demonstrate a level of personal and professional commitment to national security but also an expectation from the national government that Dr. Huber would alert appropriate authorities in the event of a threat to the U.S. agricultural system. The testimony of these researchers is representative of a larger-scale response pattern. The USDA reactions to their request for support and recognition that their research is valid and aligned with federal goals was supported to the extent that their research "did not offend anyone", but providing conclusive evidence to the contrary resulted in the agency effectively veiling their contributions to "sound science" and silencing their voices as representatives of the federal government, thus essentially making their research invisible within the pool of "available scientific data" from which policy decisions are based.

The type of microbiology that the OECD (in 1986) suggested needed more development was microbiology oriented towards advancing the field of biotechnology. According to Kremer and Lucero their research was approved and supported by the USDA until their research outcomes countered, or rather had the potential to counter agricultural biotechnology (including agro-chemical industries) initiatives. According to

Huber, his cautionary request of the USDA was largely ignored (personal communication, June 5, 2016; https://www.youtube.com/watch?v=UDLdTXe2koo). Thus, it seems that public support for research in plant science and microbial physiology is limited to the extent that the research outcomes align with national and/or OECD goals. Between valuing microbiology for its potential contributions to further advancing r-DNA techniques and determining a level of safety from pathogenic risk, based on the assumption that if a substance is safe in one context it should be safe in another, the three microbiologists' (Kremer, Lucero and Huber) discoveries were ill-contributing to the advancement of the innovative forward momentum of the agricultural biotechnology movement. Reflecting on Samsel and Senef's (Apr. 18, 2013) article, the authors challenged industry-promoted assumptions about glyphosate's mode of action (that it disrupts the plant's capacity to access and utilize essential amino acids but does not exist in mammals and therefore does not pose as a risk to human health), by suggesting that glyphosate's impact on the shikimate pathway was not limited to plants, but also was linked with systemic hazards via mammalian gut microbiome (which utilizes the shikimate pathway).

The work of the researchers discussed above (and the work of other anonymous researchers) countered the biotechnology initiative in a fundamental way and to promote their work at the regulatory level could potentially upset the balance of a very large economy-driven system. Considering the widespread global applications of glyphosate formulations, major market economies and trade relations would be significantly impacted by precautionary measures based on alternative safety assessments. However,

as discussed in chapter 4, Dr. Huber pointed out that if precautionary measures are not taken, these markets will be negatively impacted anyway and public and environmental health will be increasingly threatened.

Although these scientists have found it challenging to conduct and share their research at the federal level, they have been actively engaged at the public level, sharing their research and providing an opportunity for knowledge exchange. But the societal impact of their research remains within the public tier while the government policy tier continues to use outdated standards that hinder the progression of scientific revolution as a national priority, thus suggesting that perhaps the priority is not Science, but a science that produces limited, predictable policy-related outcomes. “Sound science”, as is often used in political discussions regarding the validity of scientific research-supported policy, refers essentially to a partial science. In other words, the data available to the system seems to be validated if the outcome meets a particular need. This can be concluded by reflecting on, for example, EFSA and USDA claims that new evidence does not override the previous conclusions of safety. This type of system is not well-suited to change because the scientific methodologies and inputs are standardized, which has been shown in the multitude of industry-supported studies to produce predictable results. For example, during the beginning stages of agricultural biotechnology policymaking and regulatory development, U.S. government promoted industries to provide the data required for safety assessments. At the same time, federal funding for public research was being downscaled, thus limiting the amount of publicly available research. Patent rights protected industry, to a great extent, from independent research, thus limiting

independent studies from the available pool from which policies and regulations were drawn from. Therefore, government agency and health organization use of "weight of evidence" allowed for an industry-weighted data pool in determining food and chemical safety. E.C. policy shifts that allowed certain chemicals to be evaluated according to U.S. standard protocol allowed this system to influence E.C. determinations of safety as well.

The regulatory and policy-related barriers to external (non-standardized) scientific input creates a loop that resists change and thus, continues to support those who designed and depend on the system for validation and credibility of a specific process and outcome. Change in this system is limited in order to maintain a specific economic and ideological perception of productive and desirable output. The recent negative attention drawn not only to glyphosate and its accompanying adjuvants (e.g. POEA's) and the discovery of unexpected effects of transgenic technology highlights the limited scope and function of this system. Expanding the scope and function of this system to incorporate alternative outcomes, however, threatens to dismantle the validity of the partial science, which in turn threatens to crumble the foundation upon which several current food and agricultural regulatory policies rest and a significant portion of agro-chemical and biotech seed industry depends.

Public and independent researcher's such as Huber, Kremer and Lucero are integral not only in working with new crop varieties, but also in filling in the gaps with the current U.S. agricultural system. They are also valuable contributors towards a scientific revolution in terms of discovering, exploring and validating new paradigms. But they're contributions to furthering the breadth and depth of our understanding of

plant and soil health, glyphosate and agricultural biotechnology remains noticeably quiet in publicly accessible government publications. Their research papers are available but it seems that the only discussion available online is from radical anti-GMO groups, which is where I learned of these three researchers. Initial U.S. and OECD policies and regulations that were based on assessments of safety and subsequent determinations of GRAS and substantial equivalence were qualified with statements such as "…future scientific development will lead to further refinement" and "regulatory regimens could be modified to reflect a more complete understanding of the potential risks involved" (OSTP, June 26, 1986, p.4; see Ch. 4, Developing Standards: defining roles).

As independent and public research began to populate the pool of glyphosate, POEA, Roundup, NK603 and other transgenic crop studies, the weight of evidence has begun to shift and the initial determinations of safety is no longer firmly tilted in favor of glyphosate, Roundup and herbicide tolerant crop safety, which raises the question of how knowledge is developed, validated and disseminated in regards to economic and political security. This point was raised by Dr. Huber in his letter to Tom Vilsak, in which he expressed grave concern about the potential economic (and political) consequences, as well as the social consequences of preventative action verses inaction in reference to a hazardous plant pathogen linked to glyphosate/Roundup and transgenic crops. Perhaps a look at the OSTP "Guidelines" might offer some kind of explanation for Vilsak's response (or, lack of) response. The OSTP "Guidelines" offer federal agencies a means to shield from the public certain research that might be considered "influential" (i.e. containing information that "could have or does have a substantial impact on important

public policies or important private sector decisions". This type of research requires "additional quality checks beyond peer review" that determine whether federal agency research could be disseminated to the public. The additional quality checks referred to in-house peer review and the Guidelines provide a list of criteria to determine the credibility of in-house reviewers (see Data Restrictions). However, glyphosate, Roundup, NK603 and a multitude of other transgenic crops had already been approved by unpublished, non-peer-reviewed research. Thus, the scientific data available to the system to support initial (and subsequent) regulations and policies is not based on these guidelines. Perhaps the basis for policies and regulations, if not based upon appropriately peer-reviewed data, is based upon whether the research and data encompass the goal of the National Science and Technology Policy Organization and Priorities Act of 1976 and the Stevenson Wydler Technology Innovation Act of 1980's—data that promotes the ideologies of national security and global leadership through advancements in biotechnology. Kremer's discussion regarding how USDA-ARS research projects were determined according to national goals and Lucero's comment about how her research would never be supported because it did not promote the bio-agriculture chemical companies, suggests that perhaps the results of Kremer's, Lucero's and Huber's (et al) research did not fall in line with national objectives, and therefore, did not qualify as valid input and therefore was not qualified to influence policy or regulatory change. From a social construction perspective, this rejection creates an insider/outsider environment that excludes the data that might expand the boundaries of U.S. reality. Maintaining this separation, government policies and regulations remain supported by the limited scientific processes and the

resulting evidence that, in turn, define perceptions of safety which then determine the need for further research. Within this logic, scientific revolution is repressed within the "official" system, but, as Huber, Kremer and Lucero illustrate, intellectual property and patent rights are limited in their capacity to restrict scientific development. Regardless of government validation (i.e. validation through policy utilization), public and independent scientists continue to evolve perceptions of reality and periodically challenge the standardized perceptions of validity. The barriers, however, between public/independent scientists and government decision-makers restrict interpretation of the research to the decision-makers and, for now, limit the realities constructed from that research to the socially constructed boundaries of policymakers and industry representatives.

Cultural Perceptions

The "great debate" between the European Union and the U.S. revolves around local to international economic, political and cultural issues. Persistent questions regarding the validity of scientific methods, data and data interpretations seem to have formed the basis of uncertainty for all sides of the conflict. Underlying these, however, are the distinctions between socially defined concepts of security. Recall Week's (1994) suggestion regarding how conflicts are likely to arise when one party's needs are perceived as incompatible with another's. Add Diamond and McDonald's (1996) concept of power politics and one can see how parties enmeshed in a relationship based on supporting each other's economies (through the promotion and movement of key commodities) might become entrenched in conflict if the values of those commodities

diverge to the point where the parties' security (cultural and/or economic and political) feels threatened.

Underlying these differences in commodity values, divergent perceptions between scientific interpretations play a significant role in the ongoing conflict surrounding genetic engineering and they ring of clashing socially constructed boundaries of reality and scientific revolution. In other words, within the boundaries of what is known to us (whether it is our own research, our own values, our own experiences) perceptions of risk stemming from those "knowns" derive from something familiar and are driven by a "future" that is supported by one's particular experience with the past. Discussing what is known to "us" and what is known to "them" in conjunction with the futures envisioned from each perspective has the potential to further define barriers between "us" and "them", thus exacerbating conflict. But, it also has great potential to stretch personal boundaries of reality, enabling one to reflect upon one's own risk in terms of another's endeavor.

The points Salomon Wald suggested in 1996 are still used by proponents of agricultural biotechnology. This is evidenced in the Nobel Laureates' letter to Green Peace and implies a superior alternative to traditional agricultural practices—alternatives that are healthier for people and the environment (but which do not address underlying social, political and economic contexts that contribute to environmental damage, nutritional deficiencies and global hunger, or the time, effort and financial investment spent addressing these issues). While Green Peace's response raises valid points regarding nutrition, food equality and the current status of one transgenic product, the

language takes on an “either-or”, “win-lose” “good-bad” tone that devalues the positive efforts, accomplishments and intentions of the opposing party.

The recognition, time and resources allocated towards “biotechnological innovation” that started in the 1970’s has followed a narrowly defined path towards what the U.S. federal government perceives as national security, food security and scientific progress. Compared to the U.S., the E.U. has not aggressively promoted agricultural biotechnology within its member states but has held a more cautious approach to introducing transgenic products within its borders.

Considering the extensive negative feedback that Séralini and his research team received after submitting evidence to the contrary (i.e. evidence of potentially hazardous toxicity where other research indicated otherwise) of industry and policy assumption, one might understand better how the potential to protect one’s reputation, by erring on the side of, ironically, caution, might seem a feasible option. But in taking the risk associated with challenging assumptions of safety (e.g. assumptions about acute and chronic tests in determining the potential for long-term effect, the use of animals in toxicity studies to assess human health impact, separating parts from the whole product, etc.), Séralini succeeded, at the least, in raising public awareness regarding whether the current research standards and interpretations are appropriate and adequate to make broad assumptions of safety. But the public was not the only group influenced by Séralini’s claims. The EC decision to replicate Séralini’s study (but using more rats) demonstrates that perhaps there might be something to Séralini’s claim, regardless of whether the study has begun or not.

The 94 scientists (Portier, et al) who wrote a letter/article comparing the EFSA report and the IARC report and the 100+ scientists who petitioned Green Peace to stop opposing GMO's further illustrates such discrepancy in what is considered valid. Key differences between the petitions from each group illustrate the diverse context within which the overall conflict is situated. Portier's claim for validity was based on transparency (e.g. publicly available data) and scientific rigor (e.g. published, peer-reviewed data) and the claim for validity for the 100+ Nobel laureates was based on input from "[s]cientific and regulatory agencies", suggesting a level of authoritative voice supporting the viability of transgenic crops as a whole.

Conclusion

The 2016 U.S. National Academies of Sciences, Engineering and Medicine study emphasized that the issue of biotechnology, quoting the former (1999) Secretary of Agriculture Dan Glickman, "boils down to a matter of trust. Trust in the science behind the process, but particularly trust in the regulatory process that ensures thorough review" (National Academies of Sciences, Engineering and Medicine, 2016). The policy development for NK603 and Roundup is complex. It depends, in large part upon the validity of the scientific methods that support the determination of whether a product is safe or not. How science is determined as valid is determined by the integration of a multitude of economic, socio-cultural and political factors that influence how knowledge is created, transformed and disseminated between researchers, industry, governments and the public. The conflict surrounding Eric Gilles-Séralini's et al (2012), research provides a window to the broader issues of at stake with GMO policy development and pesticide

regulation. The research presented here demonstrates that in addition to stakeholder interests, transparency, trust, and balance of power are integral underlying factors driving conflicting ideologies and scientific interpretations of whether herbicide tolerant GMO's and their accompanying pesticides, are safe, or not.

Chapter 6: Comparative Analysis

Lead Arsenate, DDT and Leaded Gasoline

Introduction

Since the time of the ancient Greeks and Romans, humans have used lead for a variety of purposes such as cosmetics, paint, wine making, plumbing, tools and manufacturing. Lead was abundant and was more malleable and less corrosive than iron, making it an attractive substitute for many societal applications. However, it has also been known, since the ancient Greek and Roman period that lead is hazardous to human health, causing symptoms and complications as aggressive behavior, reduced IQ and other developmental skills, infertility, muscle weakening and fatigue, hearing loss, etc.

> The Romans were aware that lead could cause serious health problems, even madness and death. However, they were so fond of its diverse uses that they minimized the hazards it posed. Romans of yesteryear, like Americans of today, equated limited exposure to lead with limited risk. What they did not realize was that their everyday low-level exposure to the metal rendered them vulnerable to chronic lead poisoning, even while it spared them the full horrors of acute lead poisoning. (Lewis, May 1985)

By 1621, the U.S. began mining, smelting and producing leaded products, finding, by the late 1800's a new use for it as an agricultural pesticide. The Paris Exposition, in 1889, seemed to jumpstart the interest in and use of chemical applications in American agricultural practices as new pesticide application technology demonstrated easier, faster ways of combating agricultural pests (Schooley, et al, 2008). Demonstrating

the versatility of lead, its uses expanded from the agriculture to the automotive industry. Prior to the 1920's, Ford Motor company dominated the automobile market with basic, affordable cars such as the Model T that had become "the standard for the industry" (Rosner and Markowitz, 1985, p. 344). General Motors shifted their marketing focus from basic and affordable to "comfort, convenience, power and style" (quoted in Rosner and Markowitz, 1985, p. 344). Developing a more powerful engine was one of the key factors in how leaded gasoline became the foundation of this cultural transition (ibid).

Eventually, the use of lead arsenate shifted to DDT and the use of leaded gasoline shifted to unleaded alternatives. The introduction of lead arsenate, DDT and leaded gasoline, along with the research used and policies developed to support their use and eventual phase out, highlight certain patterns of knowledge transformation that are similar to those of agricultural biotechnology. The following comparative analysis is a basic look into potential patterns, i.e. it is suggestive of pattern, but not conclusive. The purpose of including it in this research is to broaden the context from the recent development of agricultural biotechnology to previous technologies that, at the time of their introduction, offered innovative solutions to real or perceived problems.

This chapter is organized in a similar manner as chapters four and five in that the same themes, as well as some of the same sub-themes, are used to compare with the current topic. The research is presented first, and apart from, the analysis, and is indicated by heading. Because it is a basic comparative analysis, the research presented offers more of a summary outline than a comprehensive data-set and the analysis offers a simplified comparison rather than an in-depth, point-for-point analysis.

Research

Theme 1: Developing Standards

Cultural Transitions

Lead arsenate and DDT. According to some, "[c]hemical control of insects is considered one of the most beneficial developments of civilization" (Codling, Oct. 3, 2011). At the time, Paris green, a copper arsenate-based pesticide (first used against the Colorado potato beetle), was widely used against the gypsy and coddling moths that were a major problem particularly for fruit crops and is known as the "first example of large-scale effective chemical control of an insect pest" (Codling, Oct. 3, 2011). But Paris green was also phytotoxic and thus hard on the plants. This was also about the time when the USDA began to develop its pest management program, land grant universities and extension programs, beginning the first government-sponsored integrated pest management programs to help farmers more effectively deal with destructive crop pests. The USDA developed and promoted pest management strategies that used a combination of chemical applications with innovative, non-chemical methods but chemical use for commercial applications outpaced the latter because it was faster, easier and relatively inexpensive (Schooley, et al, 2008). A new, more viable chemical than Paris green was introduced in 1892—lead arsenate. Because of its increased solubility, longer-lasting persistence as a residue (i.e. it did not wash away easily and, therefore, protected the plant longer) and decreased phytotoxicity it was quickly adopted worldwide as a viable, affordable, easy-to-use substitute to its "contemporaneous alternatives" (Peryea, Aug. 20-26, 1998, p. 3).

However, residues “in amounts equivalent to half a medicinal dose on an individual pear” spurred the Boston Health Department, in 1919, to refuse a shipment of fruit from western producers and in 1926, Great Britain stated it would not accept shipments of American fruit unless it met maximum residue limits for arsenic of 0.01 grain/pound of food (ibid, p. 369). Through a cooperative effort between multiple federal bureaus, an effective washing solution and method of application was developed and patented. By 1925, a certification procedure was developed through a cooperative effort between industry (funding government approved field analysts to certify fruit) and the Bureau of Agricultural Economics (to grade certified batches and seize produce that exceeded residue limits (ibid). According to Frisbie, (Apr. 1936), the FDA developed a faster, more accurate method of testing residues in 1933 and that same year the federal government passed regulation limiting residues on fruit to 0.025 grains of lead per/pound of fruit (Schooley et al, 2008; Frisbie, Apr. 1936)

A new pesticide, DDT, was introduced in 1947. It had been used widely during WWII as a highly effective means to reduce mosquito-borne illness. It was also residual (considered a positive attribute at the time as it remained on the plants longer, thus decreasing the number of repeated applications) and it was highly effective not only as mosquito control, but also as an agricultural pesticide and was soon widely adopted (Schooley et al 2008).

Leaded gasoline. The development of leaded gasoline derived from the petrochemical and automotive industries in the early 1920’s as one of several solutions to engine knock. Leaded gasoline was marketed as a means to make engines run more

efficiently and at much higher speeds than its alcohol fuel. Some studies suggested (according to the authors) that alcohol fuel was a cleaner but just as efficient fuel, making its performance superior to gasoline, albeit more expensive, alcohol fuel was heavily promoted just prior to its discovery (Rosner and Markowitz, 1985).

However, just prior to the introduction of leaded gasoline engines, in 1921, Thomas Midgley, a General Motors Research Laboratory chemist and DuPont had been promoting alcohol fuel as having all of the positive attributes that they would later claim leaded gasoline had—except for the cost (Rosner and Markowitz, 1985; Needleman and Gee, 2013). But in 1922, Midgley helped develop leaded gasoline for which DuPont supplied a study for General Motors indicating that when/if petroleum supplies diminished, alcohol could be easily substituted.

Defining roles—leaded gasoline

Standard Oil Company, General Motors and DuPont Chemical Company (the latter two also formed the Ethyl Corporation) as well as some federal agencies/bureaus promoted leaded gasoline as a progressive industry strategy that was indispensable to the national economy and the future of the nation, which could, therefore, ill-afford to create needless regulatory barriers (ibid). As leaded gasoline became streamlined into the automotive market, consumption rates rose and the number of cars operating on leaded fuel increased. Responding to the Surgeon General's request that the US Public Health Service's Division of Chemistry and Pharmacology look into claims that lead particles could accumulate in the air along busy roads, the Division's director reasoned that because the length of time required to conduct such a study could take up to a year, it was

"recommended instead that the Public Health Service depend upon industry itself to provide them with the relevant data" (Rosner and Markowitz, p.2). In the meantime, in 1927, the Surgeon General issued a standard, voluntary tetraethyl lead guideline of 3 cc/g, which matched the standards already in place in tetraethyl leaded gasoline refineries at the time. By the 1960's, the Surgeon General had increased the (voluntary) standard from 3 cc/g to 4 cc/g. However, General Motors sold their share in the Ethyl Corporation in 1962 and soon began to phase out their dependence on leaded fuel, refocusing their production on developing catalytic converters and by the 1970's the benefits of alcohol fuel were "discovered" again.

Theme 2: Perceptions of Safety and Validity

Cultural Perceptions

Lead arsenate and DDT. The more lead arsenate was used, the more resistant pests became which resulted in higher application rates and, consequently, higher concentrations of lead and arsenic on produce and in the soil (Peryea, Aug. 20-26, 1998). Walter Frisbie, who had been the Chief of the Division of State Cooperation for the FDA and USDA wrote in 1936 that the USDA had recognized, over the previous 20 years, that the increasing use of lead arsenate, in combination with oil "binders" (which improved and prolonged the effectiveness of each application), were creating a public (national and international) health hazard.

The combination of LA and oil additives made a more residual pesticide, which was appealing for farmers but it was also difficult to wash off of produce prior to consumption (Frisbie, Apr. 1936). In 1935 there were 338 seizures of shipments that were

not in compliance. Frisbie (ibid) noted that the increasing number of seizures indicated that industry was not taking the regulations seriously. In addition, according to Frisbie (ibid), the FDA was discouraged, noting that some state officials showed "reluctance…to require the observance of a tolerance for the intrastate distribution and sale of sprayed fruits and vegetables" until each state enforced the federal standards for residue limits of lead and arsenate, "the public will never be entirely protected" (ibid, p. 371). Between 1919 and 1947, U.S. farmers and federal researchers sought new, safer and more viable solutions but in the meantime, according to Schooley, et al (2008), despite its known hazardous toxicity the rates of U.S. consumption of lead arsenate rose from approximately 29 million pounds in 1929 to approximately 86 million pounds by 1944 and fell to just under 4 million pounds by 1973.

Use of LA began to fall during WWII, when lead became an important military resource, thus decreasing its public availability and cost effectiveness (Peryea, Aug. 20-26, 1998). Schooley et al (2008) noted that a national phase-out of the agricultural use of leaded arsenate in the U.S. began around 1950. However, even though subsequent studies demonstrated that lead arsenate was oncogenic, mutagenic, teratogenic and fetotoxic and acutely toxic, it was still approved by the EPA, as late as 1986, as a growth regulator in grapefruit and wood production (EPA, Dec. 1986) and was not banned nationwide until 1988. In 2005, the EPA listed lead and arsenic as the "top two substances on the…biannual list of hazardous substances…; they've held that ranking for the preceding ten years" (ibid, p. 33).

Although DDT is still considered one of the most effective mosquito controls and is still used in areas prone to malaria outbreaks, it's use in U.S. agriculture was short lived as Rachel Carson's landmark research and subsequent book "Silent Spring" revealed the toxic systemic impact that DDT has on the surrounding ecosystem. But agricultural chemical industry interests, according to the author, dismissed her as being hysterical, emotional, and a scientific amateur (http://www.environmentandsociety.org/exhibitions/silent-spring/personal-attacks-rachel-carson). As will be discussed further below, although a handful of toxicology studies on the effects of DDT on animals and humans had been published by 1947, the 1960's marked a distinct shift in the development of science. However, it was really the "technical developments in analytical chemistry during the 1950s" from which Carson's 1962 conclusions are based (Bouman, Bornman, van den Berg and Kylin, 2013, p. 242). By 1972, DDT was banned in the U.S (https://www.epa.gov/aboutepa/ddt-ban-takes-effect). In 1975, the EPA published "DDT: A Review of Scientific and Economic Aspects of the Decision to Ban Its use as a Pesticide" in which the majority of toxicology studies cited were from the 1960's. Subsequent research, from the 1960's and since DDT has been banned as a U.S. agricultural pesticide, has revealed that DDT is linked to a multitude of serious health issues ranging from "breast cancer, diabetes, decreased semen quality, spontaneous abortion, and impaired neurodevelopment in children" making its continued use a controversial dilemma (quoted in Bouwman, Bornman, van den Berg and Kylin, 2013). It is still used today, however, in the absence of a more effective means of controlling mosquito populations and, thus better controlling mosquito-borne diseases.

Leaded gasoline. According to Rosner and Markowitz (1985), the campaign that began in 1922 to promote leaded gasoline as the answer to quieter, more powerful engines effectively diminished the attributes of the cleaner, less toxic, equally efficient alcohol fuel that the general public could even make. Midgley subsequently claimed (despite warnings from independent and government researchers about the potential public health threat) that leaded gasoline was "the only material available which can bring about these [antiknock] results…and unless a grave and inescapable hazard exists in the manufacture of tetraethyl lead, its abandonment cannot be justified" (quoted in Rosner and Markowitz, 1985).

Weight of Evidence

Leaded gasoline. During the initial stages of integrating leaded gasoline into the American market, a multitude of questions were being considered regarding how to assess the potential health hazards associated with its use (ibid). According to Rosner and Markowitz (1985), questions such as:

> What should constitute adequate proof of safety or harm? What business, professional, or government agencies should be responsible for evaluating possibly dangerous substances?...Does industry have to prove a new substance safe or do public health experts have to prove it dangerous? In the face of scientific uncertainty concerning the safety or dangers posed by leaded gasoline, and the perceived need for this substance by the automobile industry, the broader question became: What was the level of acceptable risk that society should be willing to assume for industrial progress? (p. 344)

Hayhurst supported the Bureau of Mine's report in an American Journal of Public Health editorial in which he claimed a general scientific consensus, based on 27 months of public use with no evidence of "mishaps and poisonings", that there was no public health risk from leaded gas.

However, according to Stone (2002), public interest in alternative fuel began to shift by the 1950's with increasing awareness of urban congestion. Stone (2002) emphasized that this awareness contributed to the development of a mass transit program that would increase transportation efficiency. It could also potentially be contributed to the one of the reasons that lead arsenate was phased out—WWII resource demands may have increased the cost and the transition simply took longer than simply switching from one product to another (i.e. replacing engines was a bit more costly, times-taking and resource dependent). Further shifts in public interests, toward fuel efficiency, were spurred by the 1972 Oil Embargo as fuel shortages created a sense of crisis within the U.S.

Conflict of Interest and Public Trust

Leaded gasoline. The Bureau of Mines report (discussed above) suggested that there was no public health risk associated with the use of leaded gas in automobiles. However, scientists and researchers (Cecil K. Drinker, Dr. David Edsall, Alice Hamilton and Yandell Henderson) criticized the study as inadequate and challenged the credibility of the outcomes, emphasizing the industry's capacity to influence the data and the subsequent doubt regarding the integrity of the federal Bureau of Mines in protecting public health (Rosner and Markowitz, 1985). According to Needleman and Gee (2013),

Dr. Hayhurst (industrial hygienist for the Ohio Department of Health), had expressed in a letter to the Public Health Service that although he shared some of their concerns regarding the health hazards inherent in lead exposure, he justified countering proposals to ban its use, stating: “I am afraid human progress cannot go on under such restrictions…if we are to survive among the nations” and the argument stop its public use (as one of the Public Health Scientists had suggested) because it is hazardous to human health “might also be applied to the thousand and one other poisons and hazards which characterize our modern civilization” (quoted in Needleham and Gee 2013, p. 53). It should be noted, however, that Dr. Hayhurst not only worked for the Ohio Department of Health, but was also an Ethyl Corporation consultant whose “correspondence [with] the Public Health Service [indicated] that Hayhurst was supplying advocates of tetraethyl lead with information regarding the tactics to be used by their opponents” (Rosner and Markowitz, p.4).

Robert Kehoe, a University of Cincinnati toxicologist, spoke in favor of the Bureau’s conclusion and shortly thereafter was offered to direct DuPont and General Motors’ C.F. Kettering laboratory and soon after that “became a corporate officer at GM and a consultant to DuPont” (Needleman and Gee, 2013).

Data Interpretations

Leaded gasoline. In 1965, geologist Clair Patterson challenged Kehoe’s claim regarding “normal” lead levels in the body by demonstrating how dramatic global increase (over 600 times) in lead levels since pre-industrial times has significantly increased the “normal” level of lead and suggested that “typical” level would be a more

appropriate term. Patterson published his findings in Archives of Environmental Health and was criticized by toxicologists for crossing the boundary between his geological expertise and societal health implications (i.e. science and public policy/social application) (Needleman and Gee, 2013). However, in 1966, the Surgeon General and certain members of the Senate began explicitly questioning the impact that low level, long-term exposure to lead was having on women and children and inquired about potential alternatives if leaded gas was found to be toxic (Needleman and Gee, 2013).

Theme 3: Data Gaps

Lead Arsenate and DDT

Searching "lead arsenate" between the years 1900 – 2016 on ProQuest's Toxline for scientific research resulted in 57 articles, the earliest of which was published in 1949 and the majority of which were published after 1970. A search on ProQuest's Biology Database for "lead arsenate", for the years between 1900 and 1970, produced two results, both of which were studies of how lead arsenate affected insects. Similarly, prior to Rachel Carson's work, DDT had been studied mainly for its effectiveness as an insecticide (similar to the majority of early glyphosate studies).

Leaded Gasoline

According to Needleham and Gee, 2013, the Surgeon General had asked Midgely, in 1922, if the impact on public health from the introduction and use leaded gasoline had been considered. Midgely's response was "very serious consideration…although no actual experimental data has been taken" (ibid, p. 50). According to the authors, regardless of behind the scenes tactics that may have impacted how industry responded to

opposing arguments, scientific evidence to the contrary of the Bureau of Mines findings, at the time, was not conclusive in regards to linking exposure to lead from leaded gas with hazardous chronic toxicity and many health officials supported its continued use until it was undeniably proven to be hazardous (Rosner and Markowitz, 2013; Lewis, May 1985). The Surgeon General, after holding a stakeholder conference to discuss the risks and benefits of leaded gas, assigned an investigatory panel to determine the extent to which lead might be hazardous if it were widely disseminated throughout society (Rosner and Markowitz, 2013). However, the panel was given a seven-month timeframe in which to conduct their study, thus the outcome, according to the author, was not conclusive and could only definitively determine that there were "no good grounds for prohibiting the use of ethyl gasoline...as a motor fuel, provided that its distribution and use are controlled by proper regulations" (Lewis, May 1985, p.4).

Theme 4: Data Access Restrictions

Protecting Innovation: Benefits and Barriers

Leaded gasoline. Although health officials (including the Surgeon General) and scientists warned against the health risks linked to the introduction and projected widespread use of lead and leaded fuel,

> [d]uring the 1920s, the petrochemical and automobile industries emerged as the corporate backbone of the United States. Because the acceptance or rejection of leaded gasoline had profound implications for these industries…[p]ublic health professionals found themselves under intense pressure to sanction and minimize the hazards associated with the manufacture and use of this new potentially toxic

> substance and the pages of the *American Journal of Public Health* were compromised during the months and years when the fate of leaded gasoline was being decided… Rosner and Markowitz, 1985, p.1

Transitions: Public to Private Research

Leaded gasoline. But, for the following several decades since the Surgeon General's determination that the results of its initial 7-month investigatory panel's results were "preliminary", safety studies were essentially solely conducted by industry and industry- backed researchers (Needleman and Gee, 2013; Lewis, May 1985; Rosner and Markowitz, 1985). According to a case study on industry reactions to early scientific warnings, the:

> relevant studies…on the health effects of lead in petrol… were conducted and funded exclusively by the Ethyl Corporation and General Motors for over 40 years, and General Motors controlled the publication of results and imposed tight reporting constraints on the regulating US Bureau of Mines. [C]ritical independent scientists had their funding withdrawn and their jobs and lives threatened. (Needleman and Gee, 2013, p. 71)

Unpublished Data

Leaded gasoline. Funding the U.S. Bureau of Mines to the conduct safety study, General Motors Research Corporation/Ethyl Corporation responded to the request for safety data, requiring (contractually) that preliminary results of the U.S. Bureau of Mines' study not be shared with the public and that the study outcomes be discussed and approved prior to publication (Rosner and Markowitz, 2013).

Concluding Remark

The lack of published scientific data, in terms of toxicity studies or human health impact for both lead arsenate and DDT, prior to the 1950's, made it a challenge to conduct a brief review that could be used to compare with the knowledge development and policy processes of Roundup/glyphosate and NK603/GMO's. However, the data I did obtain, illustrated certain key points that served as a general basis for analysis. Reflecting on the history of lead use in global society, Needleman and Gee (2013) discussed Benjamin Franklin's observations in 1918 (four years prior to the initial marketing campaign for leaded gasoline) of the widespread uses of lead throughout society and the consistent patterns of subsequent negative health symptoms that accompanied lead exposure; the authors included a quote from Franklin who concluded that "this mischievous effect from lead is at least 60 years old; and you will observe with concern how long a useful truth may be known and exist, before it is generally received and practiced on" (p. 49).

Analysis

Theme 1: Developing Standards

Cultural Transitions

Lead arsenate and DDT. It could be argued that finding ways to reduce or eliminate pest problems in agriculture dates back to the beginnings of cultivated farming. Societal dependence upon the success of its agricultural system meant that the persistence and resilience of various agricultural pests was perceived as a threat to that system and thus necessitated continuous efforts to find solutions that would diminish this threat as a means to strengthen crop viability. Improving crop production was balanced in terms of the cost of input and the increase in profit, thus, securing one's time and financial investment was a key factor in determining the viability of a pesticide. The use of lead arsenate grew out of these efforts as a perceived better alternative to a previous solution in terms of addressing the pest problem and increasing crop viability. Contrary to a key marketing point for glyphosate, consumer health was not the priority issue with selecting lead over copper, but rather the attributes that made one more effective than the other in terms of its intended use. With new, easier application technology, applying chemical pesticides was a more convenient method than the manual, less expensive (and less toxic) non-chemical techniques offered by the newly-formed USDA. Convenience, in this sense, took priority over economics and health. But lead arsenate was appealing not only for its convenience, but also for its resilience (due, in part, to its accompanying oil binders), which contributed to its perceived affordability.

Lead arsenate's residual nature was marketed as a benefit and crop spraying was marketed as indispensable in terms of crop protection, but over several decades of use, there was growing public concern about how difficult it was to wash the residue off and, subsequently, how much residue the public was ingesting and otherwise exposed. The focus then transitioned from its benefits, to finding solutions to the problems created by those benefits. Residue levels became an important factor in transboundary commerce and this prompted the government to find alternative solutions (e.g. the FDA developed a washing system to reduce pesticide residue when crops came out of the fields) to help resolve the health hazards inherent with residual levels of lead on post-market products. In addition, the federal government issued regulatory parameters for interstate commerce, but, as the FDA noted, intra-state commerce did not always comply with federal standards. Public health was not a direct influential factor within the commercial market system, but increased public awareness and subsequent public resistance to products sprayed with lead arsenate could be perceived as an influential economic factor. Increased consumer resistance combined with the increased cost of lead (as a consequence of limited war-time resources) and the need for increasing amounts of lead concentration (as a consequence of pest resistance) began to make lead a less economically viable solution. There is a similar thread with glyphosate as pests are becoming resistant to it, thus requiring increasing amounts of chemical application to maintain effective pest control. Eventually, another solution developed that promoted a shift to a different pesticide. DDT did not have the long-history of health hazard that accompanied lead use but it was still resilient and it was considered a broader (thus more

convenient) insecticide than lead. In addition, the resource demands of WWII increased the cost of lead arsenate, making a transition to DDT not only more convenient and assumedly safer, but also more affordable.

Leaded gasoline. Addressing pest problems in agriculture has been a persistent thread throughout the text. The strategies employed (since the late 1800's to today) by U.S. farmers has been influenced by the innovative products (e.g. mechanical pesticide application technologies and toxic substances) that are designed to alleviate those problems. The use of leaded gasoline was more of a strategy to increase convenience by employing technology to make transportation more efficient (in terms of a smooth running engine), faster and more powerful. Safety was, in part, considered in terms of cost/benefit between public health and financial and political investment.

Herbicide tolerant crops have been promoted as an efficient, cost-effective weed management solution that could increase production while decreasing pesticide use, which enable legislative actions that justified minimizing regulatory barriers and was later used in promoting and developing biotechnology. Leaded gasoline was also promoted as an environmental and socio-economic solution—making engines faster and more efficient and therefore increasing the nation's capacity to travel faster while conserving fuel.

Defining Roles

Leaded gasoline. Maintaining boundaries between science and the broader social context was a critical issue among toxicologists who criticized Clair Patterson for applying his geological expertise to the broader social context. Using critical theory to

analyze how knowledge generation is separated from knowledge application, we can see that these boundaries exist in the current conflict, mainly between researchers and policymakers, thus creating a communicative barrier between those who create the data and those who use that data to impact society. In addition, we also can see that the barriers that inhibit researchers from directly influencing policy decisions did not exist for the leaded gas industry just as it did not exist for the agricultural biotechnology industry. Interpretation of the data, thus, becomes a key issue in how the data is used for supporting policy and regulation.

The subsequent decades after leaded gasoline became mainstreamed, the majority of safety studies on leaded gas were conducted by the petroleum industry. Similarly, the two decades that glyphosate was registered (from 1974 to the 1990's) and approximately the first decade that NK603 was approved, the majority of toxicity studies were conducted by the agricultural biotech industry, which over time has produced an abundance of data that suggests the safety of transgenic technology and its accompanying chemical pesticide applications.

Theme 2: Perceptions of Safety and Validity

Cultural Perceptions

Lead arsenate and DDT. Similar to the theory that herbicide applications will not impact the internal microbiological processes of a plant, it was generally assumed that applied insecticides were only resilient on the crops in the field and could be washed away prior to consumption. However, as later research began to reveal that the resilient nature not only made it difficult to remove prior to consumption, it also persisted in the

soil, the economic viability of using lead arsenate began to transition, within the public and commercial market, to a liability. Although, during the widespread commercial and private use of lead arsenate of the first half of the 20th century, there was limited scientific research regarding the health hazards of lead, public observation and historical anecdotal evidence of negative health effects contributed to public resistance. From a social construction, critical theory and scientific revolution perspective, the shared experiences, ideas, needs and interests of the public began to diverge from the marketable attributes promoted by the industry. This divergence helped shift the perception of what is considered a viable solution, which, in turn helped create an environment conducive to seeking a new solution. By this time, scientific research was just beginning to reveal the systemic biological processes that would enable the public to compare, contrast and integrate personal observation and shared anecdotes with the authoritative findings of Science.

In addition to the increasing financial costs of using lead arsenate, the transition to DDT was also due, in part, to the increased resilience on the part of the pests, which had become resistant to lead arsenate applications. Increasing the application amounts of lead arsenate increased the hazard of public exposure and, regardless of federal efforts to reduce pesticide residue levels, without consistent adherence to federal residue level standards within each state, the public was still at risk. Eventually, lead use in agriculture was phased out but even with past knowledge of the health hazards associated with lead and with subsequent studies demonstrating its persistence as a soil contaminant and

toxicology studies demonstrating it acute and chronic toxicity, it wasn't until less than 30 years ago that lead was banned nationwide as an agricultural pesticide.

Lead, like DDT, persevered for its useful attributes and the lack of (available) convenient, affordable, and safer alternatives. However, as science evolved and new knowledge raised awareness (and provided an authoritative cautionary voice) of the hazardous impact, DDT was spotlighted in the midst of new a federal initiative that emphasized environmental stewardship as a national priority. Perhaps it is coincidence, but DDT was banned (in the U.S.) only two years after the EPA was created. Global use of DDT, however, further demonstrates the give and take between risk and benefit. The case for DDT differs, however, then that of glyphosate or Roundup in that DDT use shows a dichotomous measurement between health risks (known and agreed upon health hazards of using the pesticide versus known health hazards of mosquito-borne diseases) in the face of a lack of alternative solutions to the second health hazard. The case for glyphosate/Roundup is more complex, involving divergent perceptions of health risk, crop production, convenience, and perceived benefit compared to alternative herbicides.

Transitions: Basic to Applied Research

Leaded gasoline. Both leaded gasoline promoters and agricultural biotechnology promoters have marketed their respective products as having unique and superior attributes as compared to their counterpart as a means to persuade consumers to shift consumption habits. There is also a common thread between the automotive convenience/power solutions and the potential for applied research in becoming part of the problem in terms of science revealing that those solutions have a hazardous impact on

human, animal and environmental health. This relates to Kuhn's (1996) question: "What is a problem and what the solution" (p. 109)?

Weight of Evidence

Leaded gasoline. Similar to the GAO suggestion that in order to save time, the EPA should require industry to provide the required chemical safety data, the US Public Health Service's Division of Chemistry and Pharmacology's suggestion that in order to save time industry should provide the Division with the required safety data. Thus, much like U.S., E.U., WHO and FAO determinations of glyphosate safety were made amidst an industry-weighted data and/or review panels, the Bureau of Mines report was conducted and shaped by General Motors/Ethyl Corporation. However, the petroleum industry maintained that leaded gas was safe for the general public based on a lack of conclusive data indicating otherwise. This contrasts with the agricultural biotechnology industries capacity to claim the safety of transgenic crops and their accompanying pesticides, which was based on a multitude of safety studies.

Conflict of Interest and Public Trust

Leaded gasoline. Conflict of interest was a significant factor in the leaded gasoline era and is a current conflict surrounding transgenic crop and pesticide research and public policy/regulatory development. Much like Séralini, the WHO, and the ninety-six scientists who vouched for the integrity of the WHO's study and the industry-bias of the EFSA study, Drinker, Edsall, Hamilton and Henderson highlighted the industry bias in the Bureau of Mines study. The positions that Dr. Hayhurst, of the Ohio Department of Health, later held with the Ethyl Corporation is similar to the overlapping role that Diána

Bánáti played as EFSA's former chairwoman of its management board and as board member of ILSI. Regardless of individual intentions, such conflicting roles invited public speculation and doubt regarding the integrity of both the Bureau of Mines study as well as the EFSA's safety assessments and its capacity to ensure public safety. Robert Kehoe, the University of Cincinnati toxicologist who spoke in favor of the Bureau's conclusion and shortly thereafter was offered to direct DuPont and General Motors' C.F. Kettering laboratory is similar to the university professor who was hired by Monsanto and subsequently began promoting agricultural biotechnology.

Data Interpretations

Leaded gasoline. The length of study has been a common thread throughout my research. For example, Séralini's concern, regarding the limited data and subsequent interpretation that acute and sub-chronic toxicity studies can offer in terms of long-term determinations of safety, resonates with the scientists who objected to the limited timeframe (seven months) for which to study lead particulate effects on high traffic roadways. The emphasis from both was that more time was needed to conduct a thorough analysis.

In addition, the studies that supported continued promotion and public use of leaded gasoline, like the majority of studies used to support NK603 and Roundup, were industry studies (from the petroleum/automotive industry), which maintained that leaded gas was safe for the general public, just as the agricultural biotechnology industry maintains the safety of transgenic crops and their accompanying pesticides. Without evidence to the contrary regarding the hazards of airborne lead particulates, the Surgeon

General raised the lead limits in gasoline, similar to the EPA raising pesticide residue limits for various glyphosate crops.

At the time Rachel Carson's book was published, it was a fresh example of independent science that was also written and presented for public accessibility. Its popularity within the public sphere spotlighted, with conclusive scientific evidence, where the U.S. regulatory system was failing to protect the environment. It could be argued that the results of her research on the negative environmental impact of DDT influenced government response that ultimately led to its nation-wide ban. Séralini and his research team have also succeeded in gaining global publicity, but public policy change regarding agricultural biotechnology seems to be limited to the E.U. which is limited to maintaining the potential that his claim holds a level of validity (in terms of supporting a replication of his study through the G-TWYST project). In terms of assessing adjuvants and pesticide formulations, it is possible, but not directly evidenced that Séralini's et al (2012) study had any influence on the events that led to EU's ban on POEAs. Clair Patterson's challenge, in regards to what "normal" lead levels mean, offered a new element to the debate about chronic impact and toxicity thresholds, while Dr. Huber's and Dr. Kremer's research challenges assumptions of traditional microbiology and the potential for unintended, hazardous effects from transgenic plants and glyphosate interactions with soil/plant microbiomes. Samsel and Senef brought voice to independent researchers who challenged the claim that the shikimate pathway does not exist in humans and animals.

The contrast between alcohol and leaded gasoline seems to parallel, to an extent, Lucero's work with soil microbiomes as compared with chemical applications. In terms of discovering a process (in the case of alcohol fuel it was more the product) that was clean, efficient and renewable, alcohol and healthy microbiomes seem like a viable solution. However, just as alcohol was quickly disregarded in favor of petroleum products, Lucero's work, having arrived amidst established commercial success of its chemical counterparts, has also been disregarded.

Theme 3: Data Gaps

Lead Arsenate and DDT

The lack of independent studies for lead arsenate prior to 1949 illustrates how public policy was not dependent upon such research and public safety, therefore, was determined by a limited data pool. The type of research on DDT prior to the 1960's illustrates that public safety was not priority, but rather commercial application research and development. It wasn't until after Rachel Carson raised public awareness about the negative impact that the emphasis began to shift towards public health and environmental soundness. Similarly, Séralini's (et al) study raised awareness of the data gap within the current system and paved the way for public demand for independent research.

Leaded Gasoline

When the Surgeon General asked the investigatory panel to study the effects of leaded gasoline on busy thoroughfares, the panel was given a relatively short time to conduct their study even though some scientists at the time expressed that the timeframe was not long enough to conclusively determine whether or not leaded air particles were a

health hazard. The length of required studies has also been a controversial topic for current toxicity studies, as 90-day sub-chronic studies are quite often considered by industry and policymakers as sufficient to determine even long-term safety, but independent researchers and multiple advocacy groups express the need for chronic (1-2 year) studies. The result of the study, therefore, could not conclude that leaded air particulate concentrations were a hazard to human health which led to an assumption of safety that was reiterated for many years.

The lack of evidence that substantiated claims of safety between the 1920's to the 1950's began to shift as independent researchers began to develop new scientific theories and methods. The 1960's marked a change in public and government acceptance of the industry's status quo as a new scientific era as well as new technologies that enabled researchers to analyze air quality and toxicity levels began to emerge. Similarly, new scientific developments in microbiology are now enabling scientists to begin to fill in previous data gaps and to better understand the systemic interactions of microbiomes within people, plants and soils. However, unlike public policy that restricted lead use and banned DDT, the U.S. agricultural policy has remained supportive of agricultural biotechnology.

Theme 4: Data Access Restrictions

Protecting Innovation: Benefits and Barriers

Leaded gasoline. The control over which General Motors/Ethyl Corporation maintained the study, outcomes, interpretation and dissemination is reminiscent of the USDA's policies for their scientists' communication with the public regarding their

research. The experience of independent scientists whose jobs were threatened if they opposed the validity of the Bureau of Mines study and subsequent studies over the next several decades is similar to the twenty-six scientists who felt it necessary to remain anonymous in order to protect their jobs when they complained about the inaccessibility of industry materials that were necessary to appropriately conduct their studies. Reflecting on these experiences, perhaps the relationship between science, industry and government is much the same as it was then as it is now.

Concluding Remark

What does this mean for agricultural biotechnology? It appears, through this research, that the historical problem of trying to find a solution to effectively deal with weeds, harmful insects, plant disease and drought in the last century or so has resulted in only temporary relief of those problems. As science progresses and those solutions are identified as problems, significant transformation for society occurs at a large scale when that science is able to positively influence the government-industry system of policy making and regulation. The crux of the crisis, it seems, is in developing, holistic and balanced scientific data, appropriate and flexible policy and regulations, and the public resources necessary to secure our food supply safely in which the solutions used to address agricultural production needs (e.g. increasing production/decreasing loss) do not result in increasing public, animal or environmental health hazards.

If one considers the conflict surrounding perceptions of validity in agricultural biotechnology safety within context of a system, it is possible to begin to piece together how certain perceptions or actions influence others and feed the system or create barriers

that protect the system from other certain perceptions and actions. Using Figure 2 as an example, the majority of research currently used to support agricultural biotechnology policies and regulations is derived from industry research and development. The factors that contribute to this system can be linked to key events, positions, perceptions and interests and each of them contribute in ways that is beneficial to other parts of the system, which, in turn, helps to maintain the momentum and, consequently, the perception that the system as a whole, is working.

Some perceptions and actions are less influential or may even get "kicked out" of the system because they don't contribute in ways that are perceived to benefit key elements, or even perhaps, the system as a whole, which seems to be driven by streamlining economic advantage and maintaining a particular vision of political power. Consequently, these less influential or contradictory perceptions and actions take place, more or less, outside of the system and have minimal impact on current policy and regulatory decision-making. But it is here, at the fringes of mainstream science, policy and regulation, that society has a unique opportunity to view the benefits, hazards, flaws and gaps of the current system. Identifying these factors is a key step toward expanding our boundaries of reality, which, by participating in and advancing revolutionary science, has the potential to more appropriately recognize the benefits and address the hazards, flaws and gaps of the current system.

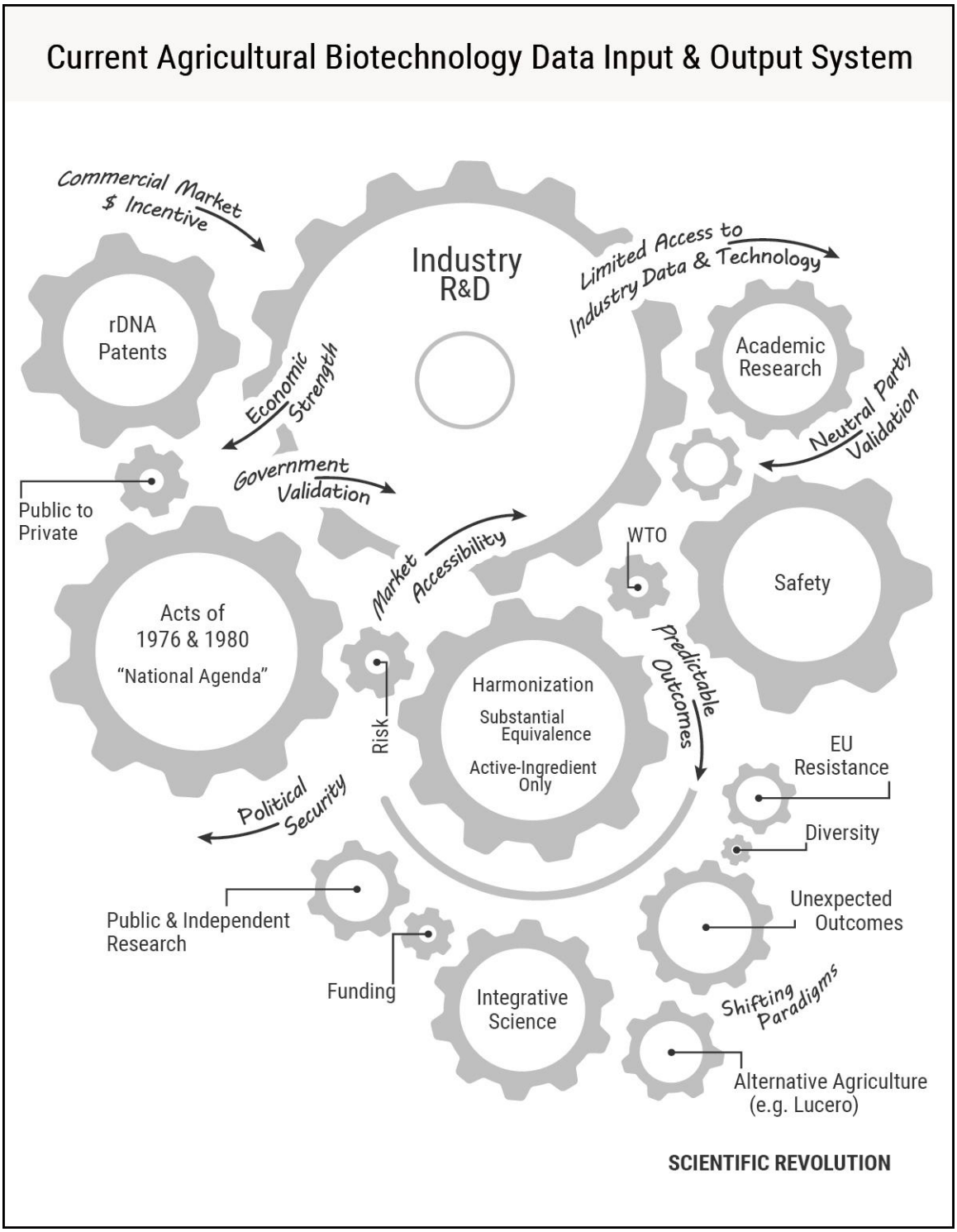

Figure 2. Current Agricultural Biotechnology Scientific Data Input and Output System.

Underlying the processes outlined in Figure 2, however, is another set of systems at work. For each position claimed and action conducted, there are underlying reasons for them and these reasons define one's interests. These interests are driven by how one perceives the extent to which options are considered valid or viable. These options are defined by one's boundaries of reality, which are, in turn, situated within the context of what one knows and trusts. At the core of one's trust, is how one determines right from wrong, good from bad—one's ethics. How one determines right/wrong or good/bad, stems from one's values which evolve from one's personal experiences. From this perspective, large-scale and complicated conflicts integrate, at every level, interpersonal processes, making small-scale, interpersonal and community-level conflict engagement a viable option to begin to address this conflict.

Weakness

What my research hasn't shown very well, is whether Séralini's et al (2012) study demonstrates a significant shift in public perceptions of the scientific validity of agricultural biotechnology toxicology testing. The data presented in my research provides evidence that Séralini's study influenced certain actions of the European Commission, thus suggesting that the study also influenced public policy-supported assumptions, but my research would have had to have included, for example, survey or interview data that specifically related public perception (regarding the above stated matter) to Séralini's work. The research presented here only offers vague inference that is not supported by specific data. In addition, the comparative analysis could have been more in-depth which would have better enabled me to make connections or differences between the subjects.

Recommendations

The value of knowledge development and scientific exploration can be measured by the willingness to identify the gaps and discrepancies and explore beyond the boundaries of what is known. The scientific breakthroughs of the scientists highlighted in this research offer extraordinary innovative value and potential economic and agricultural security for the U.S. beyond the narrow scope of the current agricultural biotechnology system. However, current federal goals inhibit the advancement of alternative agricultural systems. In addition, the democratic process ceases to be democratic when policies are developed and maintained in contrast to the majority of the civic voice. The process has become a closed loop system that inhibits new input that challenges the validity of the current output. The forward movement, the progress, the evolution of the system has become, more or less, stuck in a repetitive cycle. Inviting new input—e.g. the independent research and public voice—offers the potential to expand, change and evolve as a whole social-economic-political system. At the very least, reflection and acknowledgement of current assumptions of "sound science" and how those assumptions impact policy decisions. Along with this, parties might reflect on the underlying motives and drivers that inhibit integration of alternative scientific approaches.

My recommendation would be to increase opportunities for public civic discussions regarding underlying values and goals for the U.S. food system. Such discussions would necessitate raising public awareness of the current policies (and how/why they were developed) and the current independent and public research that supports and provides alternatives to current policies. I would also recommend public

civic discussions about the criteria of "sound science" and how those criteria are applied in the science used for public policy development and what it means for public safety. As stated in chapter two, "[r]epeated acts of political will and courage" from government level representatives will be needed to address the barriers that hinder public communication with policymakers and subsequent influence on how public policy is shaped (Diamond and McDonald, 19996, p. 30). However, considering the current national agenda, it is not reasonable to assume that Agency representatives or researchers would be able and/or willing to participate in such a dialogue if it means making certain "influential" information more transparent.

Therefore, providing an opportunity for retired and/or former Agency researchers to share their research and experiences seems like a viable strategy to begin the dialogue process. This is, in fact, how I was initially introduced to Huber, Kremer and Lucero's work. However, the venue in which these scientists met was sponsored by a group with an expressly biased perspective and anti-GMO activist intent. I would recommend a more neutral venue, facilitated, for example, by a conflict resolution practitioner with the competence to maintain a productive, positive and safe environment to explore the basis and boundaries of current agricultural biotechnology-related research. The purpose of such a venue would be to openly discuss the scientists' research (inviting former public scientists from federal agencies, independent scientists as well as social scientists and policy analysts), the personal and professional context within which that research is/was situated, how their research, in their experience, was validated and how it is situated within the context of the current agricultural system. In a sense, what this dialogue is

envisioned as is a type of Asilomar Conference in which those who attend are expected to participate openly--sharing their experiences, research and knowledge in a transparent manner. In an effort to allow the scientists an opportunity to share and discuss their stories, the conference might be best conducted in two stages: an initial session that could be publicly attended as well as live-streamed to the public but limiting active participation to public scientists and policy analysts, and a second session that invites public discussion. Conducting a conference this way would promote a public learning opportunity that could help focus the subsequent discussions. Prior to such a conference, it might be useful to offer educational resources that provide a basis for understanding the topic (e.g. the distinction between agricultural terms such as conventional, hybridization, agricultural biotechnology, organic, etc.; a description of the available biotech crops and accompanying products; a brief synopsis of the scientists' (those attending the conference) research; etc.). This information could be disseminated electronically, for example, via the conference website content and/or links. The goal of this type of conference would be to provide an opportunity to increase public understanding of the scientific data that is used (and not used) within the processes and outcomes of the current public policy and regulatory system. After such a conference, I would also recommend (to further promote civic engagement) that conflict resolution practitioners coordinate and facilitate smaller workshops that enable researchers and the public to address specific policy and regulatory-related issues by exploring the benefits and boundaries of existing and envisioned agricultural policies and practices and share the process and outcomes of those workshops with the broader public and appropriate

policymakers. Subsequent responses/actions from those policymakers would best demonstrate transparency if they are shared with the public as well.

Precaution and risk have been used quite a bit to describe the differences between the E.U. and the U.S. The evidence of risk is growing and, like Dr. Huber cautioned, it is time to assess, through serious consideration of the available research (non-industry and non-industry-funded) and discussion with the scientists themselves, "what is the problem and what is the solution". Open dialogue that not only recognizes and validates the voice and work of rigorous public/independent research but also the concerns, ideas and interests of the public is one step toward restoring the public voice within the political system. Organizing and focusing those voices provides productive opportunity for the public to become part of the process of scientific validation and, in turn, participate in the process of policy development by engaging policymakers with potential alternative solutions to help the nation reach its technology and innovation goals.

Suggestions for Further Research

Perhaps an ethnographic study of retired federal Agency researchers and their experiences with transparency, trust and validation within the Agency could lend more evidence in regards to whether the experiences of the three scientists that I highlighted in this research are unique or part of an Agency specific pattern. Such a study could potentially identify and discuss the relationship between public research, public researchers and policy development. Another study that could be potentially useful is one that looks into public access to policy development and civic engagement methods that might increase public influence in policymaking decisions.

From a science perspective, a more in-depth study into Dr. Mary Lucero's research could further develop an understanding of the potential impact that her research (and similar projects by other scientists) could have on the U.S. (and global) agricultural system(s). Such a study could analyze whether there is a potential bridge between agricultural systems (e.g. organic and bio-agriculture). Another question for further research regarding the validity of current agricultural biotechnology products (and their accompanying pesticides), is to look into the potential systemic impact of the pathogens that Dr. Huber and Dr. Kremer (and others) have linked with glyphosate interactions, i.e. if these pathogens exist in the plant, could these be influencing the toxicity tests (control and test) as well?

Conclusion

This dissertation has examined how scientific knowledge has been created, transformed and disseminated within the context of researcher-industry-government-public. I have used Séralini's, et al (2012) study as a base from which this research has grown. I have explored how research protocols have developed, how transparency and public access to information promotes and/or restricts industry, government and public interests and how perceptions influence positions and party actions. Throughout the research, I have illustrated certain patterns that reveal the systematic processes involved in current agricultural biotechnology knowledge development and how that knowledge impacts the policy and regulatory development. My research and analysis of NK603/GMO's and Roundup/glyphosate has demonstrated how science and industry influence state-level policy and regulatory development processes for agricultural

biotechnology. I have illustrated benefits and barriers of agricultural research and policy standards, demonstrating how they impact knowledge development, transformation and dissemination within the context of science, public policy, commercial application and civic participation. I think the strongest point that my research has made regarding Séralini's et al (2012) study is that it influenced the European community to take another look at the assumptions of safety regarding Roundup and GMOs.

The conflicts surrounding how science is conducted, interpreted and used for determining agricultural biotechnology safety are integrated in a socially constructed complex web that influence and are influenced by (but are not limited to) interests, values, trust, transparency, validation and perceptions of safety. Agricultural biotechnology research is grounded in the ideological perspective that humans have the potential to make things better—for themselves and others—whether by creating higher production rates, disease-resistant plants, increasing nutritional content in foods or developing a multitude of techniques to help reduce crop reliance on external inputs (e.g. fertilizer, pesticides, manual labor, etc.). The science that helped promote and support this perspective has been claimed by some as valid, safe and predictable and U.S. and international policies developed from this perspective have maintained a consistent pattern of promotion and approval of the science from which agricultural biotechnology can advance from its outcomes. But it has been shown that production rates have not significantly increased and pest resistance requires increased application rates. The technology itself, as well as its supporting products, contribute to hazardous pathogens, and chemical inputs have been increasing to compete with herbicide resistance.

Independent and public/government scientists themselves have experienced a barrier between their work and the capacity to influence how it is perceived, translated and applied in the making of public policy and regulatory standards. Knowledge development, in this sense, is compartmentalized—scientists produce and interpret specific outcomes within the context of a specific study (e.g. data and analysis from a toxicity study) and policymakers further interpret and generalize those outcomes to apply within a broader, societal context.

When the federal government has available, valid and consistent data that indicates unexpected hazardous events that negatively impact plant, animal and human health and those events are directly and indirectly linked to transgenic crops and glyphosate, at what point does a relatively stagnant technology (from a production standpoint) such as herbicide tolerant corn become a liability rather than an asset? It seems there is a valuable resource that is neglected if scientists, who know the subject, data and interpretations, are not involved, to some extent, in helping to develop appropriate generalizations and societal applications. It seems now is a critical time for such input as our agricultural system, according to the independent and public research, is potentially threatened by the solutions promoted and supported through public policy. The U.S. has an incredible, innovative resource that has the potential to make the U.S. leaders in developing a strong, adaptable and healthy agricultural system. However, that resource not only appears untapped, but also has been systematically ignored and/or rejected, thus sacrificing, to this point, not only the innovative ideas and potential applications of these scientists, but also the relationship, trust and security between

certain reputable innovators, policymakers and national representatives who enforce the current national agenda.

However, in developing innovative products or socio-political action for which require a significant amount of time, effort and money has been invested, abandoning those investments is probably not a feasible option. The question then becomes, how do we achieve this *and* that, without abandoning the core values driving each solution? The work of Dr. Kremer and Dr. Huber is (similar to Rachel Carson's), potentially, instrumental in contributing to a deeper understanding of the reasons why agricultural biotechnology has become part of the problem and thus part of the crisis. It would seem then, that the research represented by Lucero is the true paradigmatic shift that could potentially resolve this crisis. Perhaps a more in depth discussion regarding underlying values, interests, objectives and goals driving national policy development for the U.S. agricultural system could promote a baseline for further discussion about the knowledge used to develop national goals, the policies created to reach them, and the potential for alternative visions of how the U.S. agricultural system can viably support the national agenda.

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Note. This article was retracted from Food and Chemical Toxicology journal approximately one year after its publication. It has since been republished (see above) in Environmental Sciences Europe and is available via SpringerOpen Journal.

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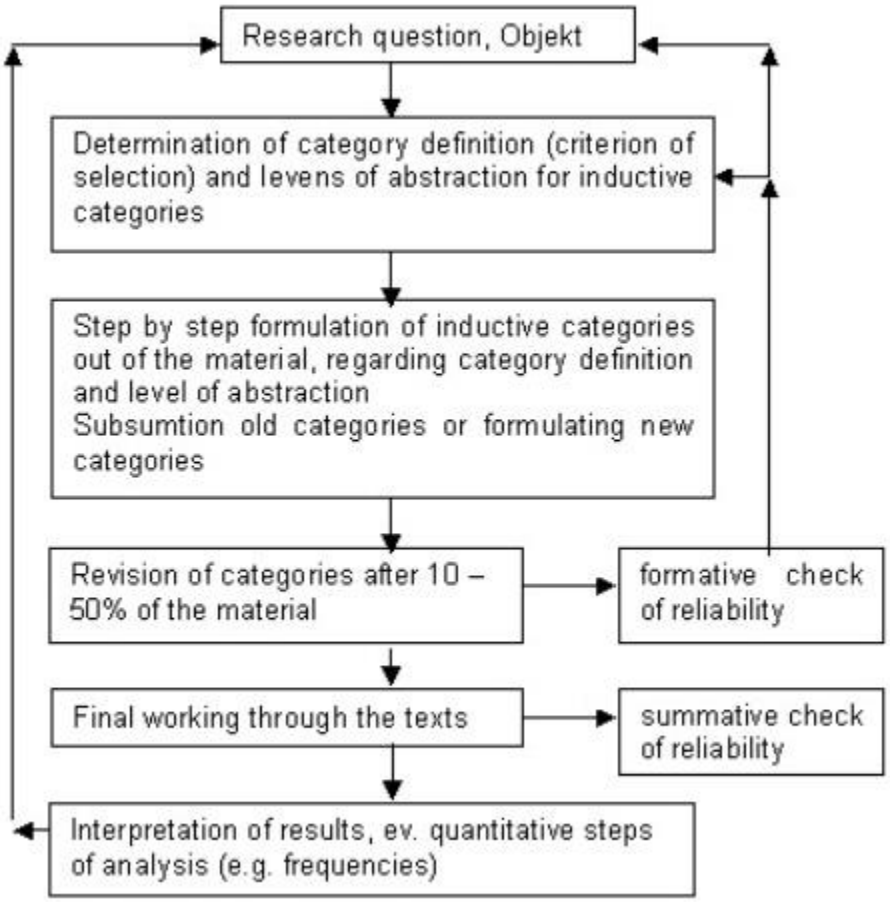
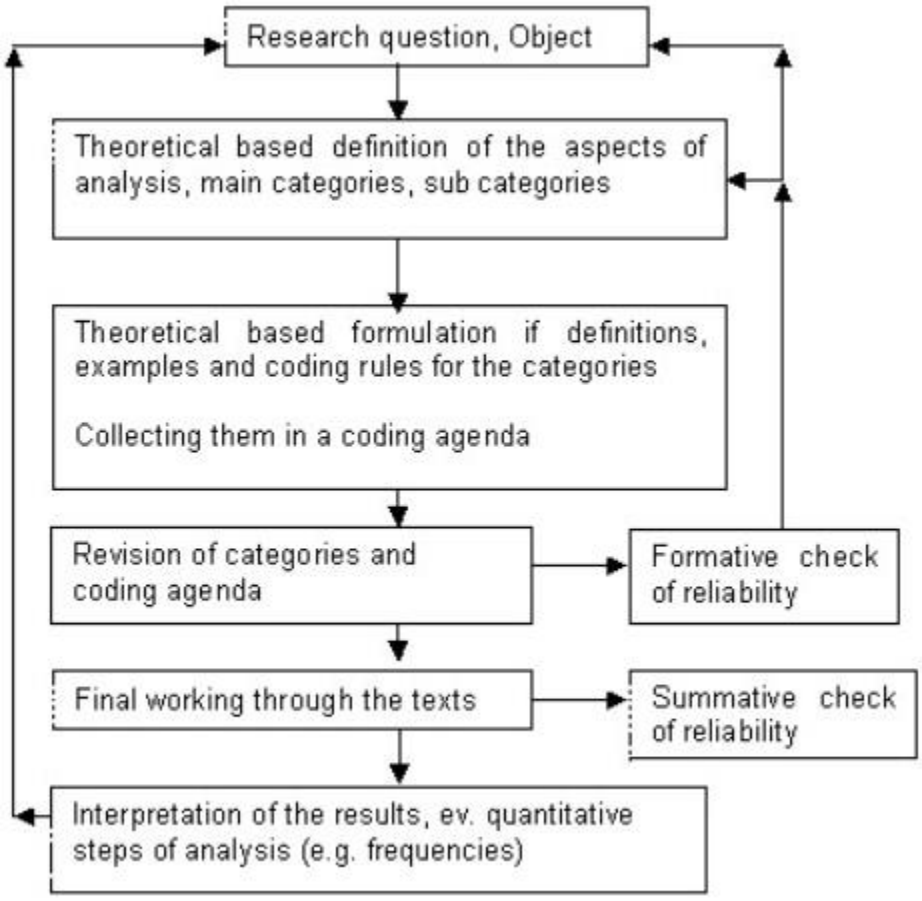
Appendix A: Inductive Coding Model



Appendix B: Deductive Coding Model



(Mayring, 2000, p. 5)

Appendix C: Interview Instrument

Dr. Robert Kremer

June 2, 2016

1. I was wondering if I could get your input regarding how your research was received by the USDA.
2. Also, if I am not overstepping my boundaries, from your experiences and observations working with the USDA-ARS, what are key factors that influence how USDA decision-makers select and validate knowledge/data for regulatory and policy change?
3. From your perspective, how does the current USDA system (of data selection, collection and use in regards to glyphosate/glyphosate formulations and transgenic crops) impact the USDA's capacity to function as a public agency?
4. How do you envision this system changing?

June 4, 2016

5. Responding to participant's comment: *Finally, a rather bothersome occurrence was that a team of USDA-ARS researchers compiled a lengthy review paper on "Glyphosate Effects on Plant Mineral Nutrition, Crop Rhizosphere, Microbiota, and Plant Disease in Glyphosate-Resistant Crops" (Duke et al. 2012. Journal of Agricultural & Food Chemistry 60:10375−10397) that had a major objective of critically reviewing my past work to conclude that evidence of the impacts of glyphosate is limited or not supported.*
   I understand why you are cautious about how your information is presented. Just curious…since you and only one other scientist (and the Brazilian) were working on the biology aspect…what were the scientists, who reviewed your work, researching?
6. Responding to participant's comment: "*Additional problematic area is the perception that how results are reported must be "inoffensive" to everyone. Statements have to be carefully crafted not to offend particular interest groups such as any agrichemical industry, or the corn growers group, or the no-till farmers group, etc.*"
   With this in mind, (pardon my straying into theoretical discussion) does this promote a less than accurate, or incomplete, understanding of the data, outcomes and interpretations? In other words, are favorable data/outcomes/ interpretations selected or more emphasized than unfavorable (when presenting with specific audiences/clients/ in mind)? Is the underlying driver—using the data to increase the breadth and depth of knowledge (with which to base informed decisions/actions) or justification?

Dr. Don Huber

May 23, 2016

1. There is a lot of chatter on the mainstream web about a letter that you had sent to the USDA's Tom Vilsack but I couldn't find any official documentation of it. Please let me know if I am overstepping my boundaries, but I was wondering if you really sent one or if the rumor-mill created it. If you did send it, would you be able to tell me what it was about and how Vilsack responded?
2. Have you attempted to communicate your research findings, and subsequent public and political implications, regarding your recent research findings with the USDA (or any other government body) prior to that letter or since that letter?
3. And, if I could press the boundaries a little further, based on your extensive experience as a publicly supported researcher, how do government regulatory policies for agricultural biotechnology reflect the general state of, and use of, agricultural science and the data generated from it? (How do your recent research discoveries relate to this?)
4. How do you envision a significant positive transformation of the current policy-making, regulatory, and/or agricultural system--i.e. what do you think it will take to shift the balance in the current system?

May 24, 2016

1. Also, in your 50+ years' experience with agricultural systems, how does this current science-industry-policy-public health relationship compare to past agricultural systems?
2. I was also wondering if you tried communicating your findings with the EPA, since they are responsible for regulating glyphosate, or the FDA, since they are responsible for post-market food safety, and, if so, what were their responses?

June 4, 2016

1. I can see your research also applying to standard toxicity tests (e.g. rodent studies) but I have been wondering how the research/design parameters and standards set up by the OECD impact a researcher's and/or policy maker's capacity to identify the hazards that your (and your colleagues') research illustrates?
2. Although the U.S. government has apparently ignored your research, how has your research been regarded by other country authorities?
3. With the current conflict regarding risk v precaution, it would seem that your work would validate a certain level of precautionary action, but again, I wonder how the parameters that define "sound science"--in the political sense--would allow certain governing bodies to include or exclude research such as yours as part of risk assessment and potential justification for risk management?

Appendix D: EPA Toxicity Memos

Glyphosate/Tox

CASWELL FILE 49

releasable

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 12 1986

004975

MEMORANDUM:

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: EPA Reg. #: 524-308; Glyphosate; miscellaneous data; one-year dog study
Record No. 162078
Caswell No. 661A
Accession No. 260021
Project No. 954

TO: Robert Taylor
Product Manager (25)
Registration Division (TS-767)

THRU: Edwin Budd, Section Head
Review Section II
Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: William Dykstra
Toxicology Branch
Hazard Evaluation Division (TS-769)

Requested Action:

Review of submitted one-year dog study with glyphosate.

Background:

A two-year oral dog study (No. 651-00565) done at IBT was evaluated and declared invalid by the Canadian Government.

The present one-year dog study is a replacement of the previous invalid two-year dog study.

Recommendation:

The absolute and relative pituitary weights of the mid- and high-dose male dogs are suggestive of a possible compound-related effect. The registrant is requested to further address the pituitary findings and the relationship to treatment.

Review:

1. Twelve month study of glyphosate administered by gelatin capsule to Beagle dogs. (Monsanto Company Environmental Health Laboratory; Project No. ML-83-137; Study No. 830116; 8/22/85.)

004975

Test Material:

Glyphosate technical; Lot No. NBP 2472136; purity 96.13%; white granular solid.

Randomized groups of six male and six female beagle dogs were fed, by gelatin capsule, dosages of 0, 20, 100, and 500 mg/kg/day of test material daily for one year.

Criteria evaluated included toxic signs, mortality, body weight, food consumption, ophthalmologic evaluation, hematology, (RBC, WBC, Hct, Hgb, MCV, MCH, MCHC) clinical chemistry (albumin, SAP, BUN, CaTT, Cl^-, Chol, creatinine, direct bilirubin, gamma-GT, glucose, phosphorus, potassium, SGPT/ALT, SGOT/AST, total bilirubin and total protein), urinalysis, (pH, protein, glucose, ketone, blood, bilirubin, urobilinogen) organ weights (adrenals, brain, heart, kidneys, liver, ovaries, testes, pituitary, thyroid/parathyroid), and histopathology of selected tissues and all gross lesions.

Statistical analyses of the data were performed.

Results:

All animals surivived the duration of the study.

Toxic signs were observed more frequently in glyphosate treated dogs than controls. They consisted of redness of ears and skin in dog 1M003 of the low-dose males, dog 2F004 of the mid-dose females, and dog 3F004 of the high-dose females. Increased incidences of abnormal stool were observed more frequently in dog 1F005 of the low-dose females and dog 3F006 of the high-dose females. These findings were not considered biologically significant since they occurred in a few dogs and were not dose-related.

Ophthalmologic findings were unaffected by treatment.

Body weight and food consumption were comparable between control and exposed dogs.

Hematological values showed occasional increased or decreased values in treated animals as compared to controls. These values occurred as increased RBC and hemoglobin values at six months in low-dose females and and increased values in MCHC in low- and mid-dose female dogs at three and twelve months.

However, the findings were within the range of control values and were not considered compound-related.

At three months, decreased sodium and potassium levels were noted in high-dose females and mid- and high-dose males. Decreased phosphorus levels occurred in low-dose females at three months and high-dose females at three and twelve-months.

These differences were within the range of control values. Other clinical chemistry results during the study were not dose-related and were within the range of control values.

Terminal body weights were comparable among control and exposed dogs.

Absolute brain weights of mid-dose males were significantly decreased. This was considered incidental to treatment. Decreased pituitary weights (absolute and relative) were observed in mid-and high-dose male dogs. Although there were no underlying histopathological changes in that organ, the individual values of the mid- and high-dose dogs were generally not within the range of control values.

Individual pituitary weights are presented below:

	Pituitary in males Weight (grams)			
Dogs	Control	Low	Mid	High
1)	0.088	0.079	0.066	0.064
2)	0.096	0.069	0.050	0.070
3)	0.076	0.090	0.061	0.055
4)	0.080	0.073	0.054	0.062
5)	0.083	0.089	0.071	0.074
6)	0.079	0.077	0.067	0.080
Mean	0.084	0.080	0.062	0.068
S.E.	0.003	0.003	0.003	0.004

Relative pituitary weight are shown below:

Percent Relative to Terminal Body Weight

Pituitary in Males

Dogs	Control	Low	Mid	High
1)	0.00073	0.00057	0.00061	0.00059
2)	0.00106	0.00056	0.00047	0.00064
3)	0.00069	0.00066	0.00053	0.00061
4)	0.00065	0.00063	0.00054	0.00061
5)	0.00090	0.00099	0.00068	0.00069
6)	0.00068	0.00066	0.00059	0.00060
Mean	0.00079	0.00066	0.00057	0.00062

Therefore the decreased pituitary weights of the mid- and high-dose males are suggestive of a possible compound-related effect.

There were no histopathological findings considered treatment-related.

The incidence and grade of microscopic lesions were comparable between control and exposed dogs.

Conclusion:

The absolute and relative pituitary weights of the mid- and high-dose male dogs are suggestive of a possible compound-related effect. Other studies with glyphosate do not show compound-related effects in the pituitary. The tentative NOEL is 20 mg/kg/day (low-dose) for this study. The registrant is requested to further address the pituitary findings and the relationship to treatment.

Classification: Guideline (tentative).

59

CASWELL FILE

Glyphosate / Tox

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Releasable
005651

JAN 12 1987

MEMORANDUM:

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Glyphosate; Roundup; EPA Reg. NO. 524-308; Addendum to one year dog study with glyphosate; PP# 6F3380/6H5502; Glyphosate in/on soybeans; revised Section F; and amended label text

Caswell No. 661 A
Record No. 186082/186083/186084
Project No. 7-0230
Accession No. 264334

TO: Robert Taylor
Product Manager (25)
Registration Division (TS-767)
and
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

THRU: Edwin Budd, Section Head
Review Section II
Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: William Dykstra 1/9/87
Toxicology Branch
Hazard Evaluation Division (TS-769)

1/10/87

Requested Action:

Review revised Section F, amended label text and addendum to one-year dog study with glyphosate.

Background:

1. PP#6F3380/6H5502

Monsanto submitted a Roundup herbicide petition that requested Agency approval to apply Roundup preharvest to soybeans. This submitted petition included a request to amend the current 15 ppm glyphosate tolerance on soybean hay to 200 ppm.

At this time, Monsanto requests to amend the submitted (2/21/86) petition by deleting the 200 ppm glyphosate soybean hay tolerance request and modifying the submitted preharvest soybean label text to restrict against feeding or grazing soybean hay or forage from preharvest soybean treated areas.

2

2. One-year dog study

With respect to the one-year dog study with glyphosate, it was previously concluded in memo of 3/12/86 from W. Dykstra to R. Taylor that "the absolute and relative pituitary weights of the mid-and high-dose male dogs are suggestive of a possible compound-related effect. The registrant is requested to further address the pituitary findings and the relationship to treatment."

The registrant is responding to that memo with this addendum.

Conclusions and Recommendations:

1. In PP#6E3424, RCB states that "RCB can reach no final conclusion regarding the likelihood that contaminants in the technical product will or will not result in a residue problem until issues involving identification/quantitation of nitrosamine presented in Glyphosate registration Standard have been resolved." This same issue regarding nitrosamines in technical glyphosate also applies to the current petition for soybeans.

Toxicology Branch requires that the identification/quantitation of nitrosamine be determined for technical glyphosate before the requested tolerances are granted.

The revised Section F has no effect on the TMRC or percent ADI utilized (review of 8/13/86 is attached). Toxicology Branch requests that RCB address the acceptability of the amended label.

2. Toxicology Branch concludes that the apparent decreases in the absolute and relative pituitary weights of the mid- and high-dose male dogs are not compound-related. The NOEL for the study is the high-dose of 500 mg/kg/day. The study is acceptable as guideline data.

Review:

1. PP# 6F3380/6H5502: Revised Section F

Proposed Tolerances

Tolerances are established for combined residues of glyphosate and its metabolite aminomethylphosphonic acid on soybeans.

40 CFR 180.364

Soybeans	6 ppm
Soybeans, Forage	15 ppm
Soybeans, Hay	15 ppm

21 CFR 561.253

Soybean Hulls	20 ppm

When used as directed on the requested preharvest application label, the soybean tolerances will need to be the following:

40 CFR 180.364

Soybeans	20 ppm

When used as directed on the requested preharvest application label, a food additive tolerance will need to be the following:

21 CFR 561.253

Soybean, Hulls	100 ppm

2. In memo of March 12, 1986, it was concluded that the decrease in the absolute and relative pituitary weights of the mid- and high-dose male dogs are suggestive of a possible compound-related effect. In response to this conclusion, the present addendum (Accession No. 264334) was submitted by the registrant. In the memo of 3/12/86 of the one-year dog study, the following data were presented:

	Pituitary in Males Weight (gram)			
Dogs	Control	Low	Mid	High
1)	0.088	0.079	0.066	0.064
2)	0.096	0.069	0.050	0.070
3)	0.076	0.090	0.061	0.055
4)	0.080	0.073	0.054	0.062
5)	0.083	0.089	0.071	0.074
6)	0.079	0.077	0.067	0.080
Mean	0.084	0.080	0.062	0.068
S.E.	0.003	0.003	0.003	0.004

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Relative pituitary weight are shown below:

Percent Relative to Terminal Body Weight

Pituitary in Males

Dogs	Control	Low	Mid	High
1)	0.00073	0.00057	0.00061	0.00059
2)	0.00106	0.00056	0.00047	0.00064
3)	0.00069	0.00066	0.00053	0.00061
4)	0.00065	0.00063	0.00054	0.00061
5)	0.00090	0.00099	0.00068	0.00069
6)	0.00068	0.00066	0.00059	0.00060
Mean	0.00079	0.00066	0.00057	0.00062

In the registrant's letter of August 1, 1986 from F.A. Ruecker, the following information is presented.

"After a review of the pituitary weight data for the 1-year glyphosate oral toxicity study in dogs (EHL No. 830116) it is my opinion that there is no conclusive evidence that the decreased mean pituitary weight for high and mid dose males can be attributed to compound administration for the following reasons:

1. The magnitude of the weight decrease is greater for the mid dose when compared to high dose (0.0222 g. v.s. 0.0162 g.) therefore there is no apparent dose relationship.

2. There is no apparent microscopic lesion present in the pituitary which would be expected to be a correlate of the decreased weight changes (atrophy or necrosis of pituicytes).

005651

3. Since the pituitary exerts hormonal control over a variety of endocrine organs, one might expect that any lesions which would reduce pituitary weights could possibly effect the hormonal output of the pituitary and thus have effects on the organs under pituitary control (thyroid, testes, adrenals, etc.). There were no weight changes or microscopic lesions observed for any of these ograns.

4. There were no comparable pituitary weight differences for females when compared to controls.

5. Finally, a review of 3 other EHL-conducted, 1 year, oral, toxicity studies in dogs (81124, 82165, 84056) showed a pituitary weight range for male controls from .064 to .072 g., and inter-group mean pituitary weight range of .062- 0.088 g., .059- 071 g. and .070-. 083 g., for each of the studies, respectively. It should be noted that the mean pituitary weights for control males (.084 g.) in the 830116 study are higher than have been observed for control males in these other studies while the mean weights for the mid and high dose males are closer to the historical mean weight ranges for controls. Additionally the mean pituitary-to-body weight ratio of .001% for each group in the 830116 study is not different from that observed in all groups in the other three studies. These data strongly suggest that the apparent decrease in pituitary weights for the mid and high dose males in the 830116 study may be actually an aberration due to an unusually high mean weight for the control males."

Conclusion:

Toxicology Branch concludes that the apparent decreases in absolute and relative pituitary weights of the mid- and high-dose male dogs are not compound-related.

The NOEL for the study is the high-dose of 500 mg/kg/day.

Classification: Guideline.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEB 2 6 1985

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Use of historical data in determining the weight of evidence from kidney tumor incidence in the Glyphosate two-year feeding study; and some remarks on false positives

TO: Reto Engler, Chief
Scientific Mission Support Staff
TOX/HED/OPP (TS-769C)

FROM: Herbert Lacayo, Statistician
Scientific Mission Support Staff
TOX/HED/OPP (TS-769C)

Herbert Lacayo Feb 26, 1985

THRU: Bertram Litt, Statistics Team Leader
Scientific Mission Support Staff
TOX/HED/OPP (TS-769C)

3/4/85

BACKGROUND

The Glyphosate feeding study (EPA Reg. #: 524-308, Caswell #: 661A, Accession #: 251007-014) on Charles River CD-1 mice generated renal tubular adenomas in male mice at the 5000 and 30000 ppm dose levels. The registrant (Monsanto) claims that such tumors are "unrelated to treatment." (ref.1). In support of that they provide historical data from Bio/dynamics and two other laboratories (ref.2).

With respect to historical data we note the large number and variety of factors which influence the life history of rodents in chronic studies. Hence, it is generally agreed that the most relevant historical controls are experiments from the subject laboratory studied within a 3 to 4 year "window" (ref.3).

SUMMARY

The main purpose of this memo is to show one way historical data may be used to evaluate the significance of tumors in the glyphosate feeding study. When these data are so used we can conclude that Glyphosate dosing has a statistically significant effect (at the p = .006 level) in the production of kidney tumors in male mice. The appropriate procedure is outlined in the next section entitled Use of Historical Data. The last Section, Remarks on False Positives, addresses some comments by Monsanto (Ref.1) on this subject. That section outlines some of the weaknesses in Monsanto's position.

USE OF HISTORICAL DATA

The following information was derived from Reference 2.

Data Source*	p (est.of tumor rate)	Sigma (est.of standard deviation)
Bio/dynamics	.00368	.00212
IRD Corp.	.00437	.00109
Combined	.00399	.00094

The value p = .00368, derived from Bio/dynamics data is a reasonable choice to use as a historical control. The data are from the same laboratory that performed the Glyphosate study and are within the appropriate 3-4 year time "window" (ref.3). Further, the standard deviation of the estimate is reasonably small.

We will now examine the Monsanto contention that the kidney tumors are unrelated to treatment. (i.e. Glyphosate has no effect on kidney tumors). First, consider the tumor rate in the Glyphosate Study: 4/198 = .0202 ---

In contrast, Bio/dynamics has the lower historical rate:

3/815 = .00368

The relevant question is: What is the probability that the 198 CD-1 mice in the Glyphosate study will produce by pure chance 4 or more mice with kidney tumors? Another way of stating this is - How likely are we to have a tumor rate of .0202 --- for the Glyphosate study given that the historical rata is .00368?

Questions of this type may be answered from manipulation of the relevant distribution which, in this case is the Binomial:

$$P(r \text{ out of } n \text{ mice have tumors}) = \binom{n}{r} p^r q^{n-r}$$

Where: n = the # of male mice in the study

r = the # of male mice with kidney tumors

p = .00368, the historical probability that an individual male mouse will develop kidney tumors.

q = 1 - p

*This does not include Hazleton Laboratories America, Inc. due to the small sample size of that data set

Using the above distribution and elementary but tedious calculations, we generate the following table:

# of mice with tumor	Probability that r or more mice will have tumors in a study with 198 male mice
r = 0	1.
1	.518177
2	.165711
3	.037443
4	.006481

This last table indicates that based on a historical rate of p= .00368 that the probability of seeing 3 or more mice with kidney tumors is about .037; and the probability of seeing 4 or more such mice (i.e. seeing what in fact happened) is about .0064. We note that even considering data from I.R.D., the p value is about .01.

Under such circumstances a prudent person would reject the Monsanto assumption that Glyphosate dosing has no effect on kidney tumor production. Another way of saying this is that if Glyphosate were truly unrelated to kidney production we would expect to see 4 or more tumors in less than 1 out of 100 experiments of the type sponsored by Monsanto. Thus, Glyphosate is suspect.

REMARKS ON FALSE POSITIVES

In ref. 1 Monsanto notes that "...if 20 types of lesions were evaluated at a probability level of .05, the number expected to be positive would not be one in 20, but rather the probability would be 64 in 100, an unacceptably high value..." Monsanto is referring to the well-known fact that by examining enough data it is likely that one will find an excess of some tumor type by chance alone; thus generating a false positive.

The Monsanto argument required the following assumptions:

1. A mouse may develop 20 distinct and independent (in the statistical sense) types of tumors.
2. The probability of each tumor type in a typical mouse is .05.

It follows from the above that:

$$P(\text{a mouse has at least one tumor}) = 1 - .95^{20} = .6415$$

Hence in 100 mice one would on the average see 64 with tumors. Monsanto proposes to avoid this "problem" of false positives by analyzing the study" ...at the .01 probability level."

We disagree with the Registrants position. First, even if one did analyze the study at the .01 level as they suggest it would still result (using the same mathematics as before) in seeing 18 mice out of 100 with tumors. And hence one still has the problem of false positives from the registrant's viewpoint. But this causes something worse from a regulatory viewpoint. We have decreased the false positive rate (i.e., the probability of saying that a chemical causes tumors when in fact it does not) at the cost of increasing the false negative rate (i.e., the probability of saying that a chemical doesn't cause tumors when in fact it does). The Registrant wishes to avoid false positives while those concerned with the public health wish to avoid false negatives. Hence, for this reason alone Monsanto's argument is unacceptable.

We further disagree as follows:

1. The two assumptions needed to support the Monsanto argument are themselves in need of support (especially the requirement for statistical independence).
2. False positive results are less likely to occur with rare tumors (ref. 5). And the tumors in question are rare.

Viewpoint is a key issue. Our viewpoint is one of protecting the public health when we see suspicious data. it is not our job to protect registrants from false positives. We sympathyze with the Registrants problem; but they will have to demonstrate that this positive result is false.

Finally, we mention that none of the tumors occurred in the control or low dose groups. Instead there was one at 5000 ppm and 3 at the 30000 ppm dose level. This together with the previous comments make it likely that there is a dose-tumor relationship for Glyphosate.

REFERENCES

1. Letter from Monsanto (signed by Frank. S. Serdy) to EPA (Attn: Robert J. Taylor) dated Feb. 5, 1985.

2. Letter from Monsanto (signed by Robert W. Street) to EPA (Attn: Robert J. Taylor) dated March 20, 1984.

3. J.K. Haseman, et al: Use of Historical Control Data in Carcinogenicity Studies in Rodents - Toxicologic Pathology - 12:126-134. 1984.

4. TOX Branch Memo from William Dykstra to Robert Taylor dated 9/4/84.

5. T.R. Fears et al: False-Positive and False-Negative Rates for Carcinogenicity. Cancer Research. 271:1941-1945. July 1977.

CFR 180.364 Glyphosate Roundup 3/12/05

File last updated 3/12/05

ACCEPTABLE DAILY INTAKE DATA **DRAFT**

RAT,Older NOEL mg/kg	ppm	S.F.	ADI mg/kg/day	MPI mg/day(60kg)
10.000	200.00	100	0.1000	6.0000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Grain Crops(64)	0.100	13.75	0.02969
Avocados(6)	0.200	0.03	0.00009
Citrus Fruits(33)	0.200	3.81	0.01144
Coffee(36)	1.000	0.75	0.01119
Grapes, inc raisins(56)	0.100	0.49	0.00074
Leafy vegetables(80)	0.200	2.76	0.00828
Nuts(101)	0.100	0.10	0.00031
Pome Fruits(120)	0.200	2.79	0.00837
Root Crop Veg(138)	0.100	11.00	0.03299
Seed&Pod veg(143)	0.200	3.56	0.01096
Palm Oil(202)	0.100	0.03	0.00005
Pistachio nuts(210)	0.200	0.03	0.00009
Asparagus(5)	0.200	0.14	0.00043
Bananas(7)	0.200	1.42	0.00426
Olives(104)	0.100	0.06	0.00009
Stone Fruits(151)	0.200	1.25	0.00374
Sugar,cane&beet(154)	2.000	3.64	0.10915
Molasses(96)	20.000	0.03	0.00920
Cranberries(44)	0.200	0.03	0.00009
Cottonseed (oil)(41)	15.000	0.15	0.03375
Kidney(203)	0.500	0.03	0.00023
Liver(211)	0.500	0.03	0.00023
Peanuts(115)	0.100	0.36	0.00054
Guava(184)	0.200	0.03	0.00009
Papayas(109)	0.200	0.03	0.00009
Mangoes(83)	0.200	0.03	0.00009
Soybeans (oil)(148)	6.000	0.92	0.08263
Pineapple(123)	0.100	0.30	0.00044
Fish,shellfish(59)	0.250	1.08	0.00406
Cucurbits(49)	0.100	2.84	0.00426
Fruiting vegetables(60)	0.100	2.99	0.00449
Small Fruit,berries(146)	0.100	0.83	0.00124
Hops(73)	0.100	0.03	0.00005
Potable Water(198)	0.500	133.33	1.00000
Tea(162)	4.000	0.07	0.00429

MPI	TMRC	% ADI
6.0000 mg/day(60kg)	1.3686 mg/day(1.5kg)	22.81

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Unpublisned,Tox Approved 2F2680,2G2686

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Soybeans (oil)(148)	4.000	0.92	0.05509
Coconut(35)	0.100	0.03	0.00005

[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible] mg/day(60kg)	1.[illegible] mg/day(1.[illegible]kg)	23.73

Current Action [illegible]

Crop	Tolerance	Food Factor	mg/day(1.5kg)
Fish,Shellfish([illegible])	[illegible]	1.00	[illegible]

ADI			% ADI
[illegible] mg/day(60kg)	1.[illegible] mg/day(1.[illegible]kg)		23.73

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 4 1985

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Consensus Review of Glyphosate
Caswell No. 661A

TO: Robert Taylor
Product Manager
Herbicide - Fungicide Branch
Registration Division

On February 11, 1985, a group of Toxicology Branch personnel met to evaluate and discuss the data base on Glyphosate, and in particular the potential oncogenic response of Glyphosate.

A. The following persons were in attendance:

Theodore M. Farber, Ph.D.
Chief, Toxicology Branch

Louis Kasza, D.V.M., Ph.D.
Pathologist

Bertram Litt, Statistician

Herbert Lacayo, Ph.D.
Statistician

Reto Engler, Ph.D.

William Dykstra, Ph.D.
Reviewer

Steve Saunders, Ph.D.

Laurence Chitlik, D.A.B.T.

The signatures above indicate concurrence with this concensus report.

B. The material available for review consisted of a package issued on January 25, 1985 (attached) and a letter from Monsanto (dated February 5, 1985), rebutting the significance of renal mouse tumors.

C. Evaluation of the Facts:

1. Long-term/Pivotal Studies:

a) A 26-month rat study showed a NOEL at 30 mg/kg/day which was the HDT. The oncogenic potential at this level was negative, corroborated by an outside consultant. Although some thyroid tumors were observed in female rats in this study they were generally discounted in their significance, in and of themselves. However, it should be noted that on a mg/kg/day basis the exposure of rats was less than 1/100 of the exposure of mice (4,500 mg/kg/day). Since a toxic, or MTD, level was not reached in this study, the panel raised the conjectural issue that at toxic levels at or close to a MTD, tumors might have been induced.

b) The NOEL in a rat 3-generation reproduction study was 10 mg/kg/day. In separate teratogenicity studies feto toxic effects were noted in rats and rabbits at levels which caused significant maternal toxicity, including death; terata were not observed (ibid). These results were, however, not entered into the discussion on Glyphosate.

2. Mutagenicity Assays:

Glyphosate was tested for mutagenic activity (1) Reverse Mutation in S. typhimurium. and E. coli with and without microsomal activation, (2) Ames Assay with and without activation, (3) CHO cells with and without activation, (4) DNA repair in rat hepatocytes, (5) Rec-assay in B subtilis, and (6) Dominant lethal assay in mice. All these tests were negative, tests 1-3 are fairly well predictive of oncogenic response while 4-6 are less appropriate. An in vivo bone marrow cytogenetics study was also performed. It was negative, but scientifically not acceptable. In summary, several appropriate and scientifically acceptable tests are supportive of non-oncogenic potential of Glyphosate.

3. In the chronic mouse study carried out by Biodynamics (#BDN-77-420) renal tubule adenomas were observed in males.

Dose (ppm)	0	1000	5000	30,000
No. Exposed	49	49	50	50
Tumors	0	0	1	3

See review of W. Dykstra (dated 9/4/84).

This is a rare tumor even in Charles River CD-1 male mice. Biodynamics historical data (included in package) show that this tumor was observed only 3 times in 14 male control groups ranging in size between 51 and 60 mice.

The probability of observing this tumor 4 times or more in 198 mice (the total number of mice examined in the Glyphosate study) is p = 0.0064 when considering the historical control of the same laboratory. Even considering other reported historical controls, the p-value is low, about 0.01 indicating that it is very unlikely that the glyphosate test group is consistent with any historical controls. (See review by Dr. Lacayo).

In addition, the response rate (see above) seems to be related to the dose.

Therefore, it was the concensus of the group that the renal tubular adenomas were related to compound administration, since their frequency was not consistent with the historical controls and there is a trend indicating dose dependency.

3a. The group noted that there were other non-oncogenic, i.e., toxicological changes apparant in the kidney and liver e.g., central lobular hepatocyte hypertrophy and necrosis and chronic interstitial nephritis in males and proximal tubule epithelial basophylia and hypertrophy in females. The group discussed the possibility of kidney irritation and formulation of crystals but noted that kidney or bladder precipitaters were not reported for this assay. Therefore, a conclusion mitigating the renal tumors could not be reached.. (See page 10 of contractor review).

D. Other Considerations:

The review panel recognizes that the exposure of mice was at a very high level 4.5 g/kg/day. Precipitation of Glyphosate in the kidneys might have occurred but none was reported. The panel believes that additional sectioning of new blocks of male kidneys might help in the interpretation of the study results. The kidney tumors as reported, were unilateral (pers. communication by Dr. Dykstra, after the panel meeting); additional histopathology could resolve the issue of whether this is a valid observation or due to not "finding" the tumors in the particular block analyzed.

The panel also believes that realistic exposure assessment, both for dietary and worker exposure are of singular importance. For example, the limit of detecting residue tolerances may overestimate exposure. Particular emphasis also should be given to residues in water, since Glyphosate has been used for aquatic weed control (EUP) and this use may become the subject of a permanent registration.

E. Classification of Glyphosate:

In accordance with EPA proposed guidelines (FR of Nov. 23, 1984) the panel has classified Glyphosate as a Category C oncogen.

ADDENDUM:

The letter by Monsanto (Feb. 4, 1985) has been considered in these deliberations. Several of the issues raised are, in fact, addressed in the above deliberations, although not point by point. A point by point rebuttal, including those points with little merit, will be done in addition to this evaluation.

Attachments

cc: B. Coberly
Caswell No. 661A

3-11-86

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

005590

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Glyphosate; EPA Registration No. 524-308; Roundup; Additional Histopathological Evaluations of Kidneys in the Chronic Feeding Study of Glyphosate in Mice.

Caswell No. 661A
Accession No. 260023

TO: Robert J. Taylor
Product Manager (25)
Fungicide-Herbicide Branch
Registration Division (TS-767C)

THRU: Edwin Budd
Head, Review Section II
Toxicology Branch
Hazard Evaluation Division, (TS-769C)

FROM: William Dykstra
Toxicology Branch
Hazard Evaluation Division, (TS-769C)

Requested Action:

Review additional pathological and statistical information on kidney tumors with glyphosate.

Background:

Glyphosate was considered oncogenic in male mice causing renal tubule adenomas, a rare tumor, in a dose-related manner. The incidence of this tumor was 0, 0, 1, and 3 in the control, low-, mid-, and high-dose groups, respectively.

Additional evaluation of all original renal sections by Dr. Kuschner identified a small renal tubule adenoma in one control male (animal no. 1028) which was not diagnosed as such in the original pathology report.

Subsequently, Toxicology Branch recommended that additional renal sections be cut and evaluated from all control and glyphosate treated male mice in order to determine if additional tumors were present.

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The results of the additional pathological evaluation of re-cut kidney sections in male mice demonstrated that no additional tumors were present. Additionally, the tumor in the control group (animal number 1028) which had been diagnosed from the reevaluation of the original slides by Dr. Kuschner was not present in the re-cut kidney sections. Therefore, the following incidence was observed.

Dose (ppm)	0	1000	5000	30,000
Renal tumors	0, 1*	0	1	3
No. examined	49	49	50	50

*Animal (number 1028) which was diagnosed by Dr. Kuschner as a renal tumor after reevaluation of original slides but not of resectioned kidney slides.

Conclusions:

The additional pathological and statistical evaluations by consultants conclude that the renal tumors in male mice were not compound-related.

This information will be submitted to the TB Ad Hoc committee for evaluation to determine if concurrence is possible.

Review:

1. Letter of September 29, 1985, Robert A. Squire, D.V.M., Ph.D., to Monsanto.

Dr. Squire has not evaluated the slides of the glyphosate study but rather the chronic toxicity data.

The following is the narrative from Dr. Squire's letter:

"The pathological endpoint in question is the presence of renal tubular adenomas in male mice. The final overall incidences were 1/49, 0/49, 1/50, and 3/50 for control, low, mid, and high doses respectively. In my opinion, these represent spontaneous occurrences rather than compound-related effects. This view is based primarily upon the biological and pathological evidence available, but is also supported by the lack of statistical significance, either in comparing proportions of animals affected or linear trend analyses."

"The following observations suggest to me that the findings in male mouse kidneys are incidental to treatment:

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"A. Historical control values in the three different laboratories indicate that, although renal tubular neoplasms are relatively rare in mice, they do occur sporadically and there is considerable variation from group to group. An analysis of these tumors should combine the adenomas and carcinomas since they represent a spectrum in development and the lesion classification is uncertain. If one does this with the Hazelton Laboratory data, there is an overall incidence of 3.4 percent tubular neoplasms which is essentially the same as the high dose animals in your study. The incidence of tubular carcinomas is not listed for Biodynamics laboratory and IRDC shows very low incidences. However, it must be kept in mind that the historical control data are derived from studies in which there were the customary one or perhaps two kidneys sections examined. If four sections had been taken from each kidney, as in your study, it is likely that historical control incidences would have been even higher."

"B. Based upon Dr. Kuschner's histopathological evaluation of the kidney slides, no preneoplastic or cytotoxic changes were evident. I know of no instance where a renal carcinogen was given at a dose sufficient to induce tumors without also inducing tubular toxicity and hyperplasia, not only in the tumor-bearing animals, but in many additional animals receiving the same exposure levels. Carcinogenesis is multi-stage process beginning with hyperplasia, and when a population of animals is exposed to a tumorigenic dose, many develop early stages of neoplastic progression even though only a few may reach the final stage, i.e., tumors. The absence of preneoplastic changes virtually precludes this being a compound-related effect."

"C. The largest and most atypical tumor in the study, according to Dr. Kuschner, was an animal in the mid-dose group (#3023). This would be highly unlikely if the tumors were compound-related since one expects the most advanced tumors to be in animals receiving the highest dose of carcinogen. Carcinogens increase not only the incidence but the degree of neoplastic progression. This is particularly true here since survival in the high dose males exceeded that of control animals."

"In summary, I feel the weight of evidence strongly suggests that the renal adenomas in male mice were naturally-occurring and not treatment related."

2. Letter of October 3, 1985, from Marvin Kuschner to Monsanto.

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In this letter, Dr. Kuschner states that he has asked Dr. Andre Varma, Chairman of the Department of Community and Preventive Medicine and a well-known biostatistician, to examine the data.

The narrative of Dr. Varma's letter of October 10, 1985 to Dr. Kuschner is presented below:

"Statistical Analysis

"A chi-square analysis of these data is not valid, because the necessary assumption of an approximate normal distribution is not valid with these small numbers. The exact Fisher's tests to compare the mice fed glyphosate with the control group is valid, but does not allow one to study the possible dose-response relation. A probit-type analysis is more appropriate with the low responses. Furthermore, there is a borderline response of one tumor in forty-nine (49) mice."

"I have decided to use a randomization test to study the dose-response. The experiment is treated as an occupancy problem. A total of five (5) tumors were observed among the male mice. I will assume that the chance of the four groups of mice is proportional to the number of mice in the group under the null-hypothesis of no effect of the glyphosate. Thus the chance of a tumor in the control group and in the 1000 ppm group is 1/49 and 1/50 in the 5000 and 30,000 ppm groups."

"Table 1 list all the 56 possible distributions of the five tumors in the four groups of mice and the associated probabilities. The chance of observing the "1 0 1 3" configuration of tumors is 0.020127. The chance of observing configurations as rare as this one or with smaller probabilities, i.e., all configurations with $p \leq 0.020127$ is 0.414134. The "1 0 1 3" configuration is therefore, not a rare event."

"I am using the following criteria to conclude that a configuration corresponds to a dose-response."

1) No response in the control group.
2) No higher response rate at a low dose.
3) No lower response rate at a higher dose.

"Using these criteria the following configurations are considered to indicate an increasing dose-response to the preparation:"

0 0 1 4
0 0 2 3
0 1 2 2
0 1 1 3

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"The sum of the corresponding probabilities of these four configurations is 0.065720. The 1 0 1 3 configuration is not considered to indicate a dose-response according to the criteria listed above. If its probability is added to the set, the total chance of dose-response permutations becomes 0.085847."

"Based on the analyses outlined above there is no evidence of a statistically significant trend in the proportion of mice with renal tumors as a response to the dose of glyphosate in their diet."

3. Letter of October 7, 1985, from Robert E. Olson, M.D., Ph.D. to Monsanto.

The narrative of the letter is presented below:

"In response to your letter of September 16th asking me to evaluate the glyphosate mouse kidney adenoma study, I am pleased to respond. Let me begin by saying that the evidence for carcinogenicity of glyphosate in mice is unconvincing. A few of renal adenomas were found in male but not female mice given very large doses of the compound, i.e., 5,000 and 30,000 ppm in the diet, corresponding to 0.5 and 3.0 percent of the diet. The distribution of tumors in the three groups of male mice studies were 1/49 in the control group 0/49 in the group fed 1,000 ppm, 1/0 in the group fed 5,000 ppm, and 3/50 in the group fed 30,000 ppm. There were no tumors in any of the female mice. These data suggest that the appearance of these tumors is random and not dose-related."

"I am further impressed by the fact that a restudy of kidneys from mice in the study by Dr. Kuschner, a world-famous pathologist, has confirmed the original findings and found no new tumors, despite the fact that three additional sections per kidney, per mouse, spaced at 150 microns intervals were evaluated. This indicates that the density of tumors in both experimental and control groups is very low and supports the view that these are spontaneously developing tumors at a very low frequency."

"When one examines other control groups, one finds that the renal adenoma is not a rare tumor in untreated mice of the same CD-1 strain and that in seven studies by Biodynamics over the past several years, renal adenomas have been observed in the control groups in two of these studies--Study A (1/54 or 1.9 percent) and E (2/60 or 3.3 percent). The control group incidence in comparable studies by International Research and Development was 0 to 1.4 percent, and at Hazeltine, the control mice exhibited this tumor at rates of 7.1 percent (1/14)."

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"In summary, it is my view that these findings do not support the view that glyphosate is oncogenic in mice. These results would not be accepted by any peer-review journal as evidence of carcinogenicity. To me, it represents a negative result, which would not be regarded by any scientific group or reputable agency as evidence of carcinogenicity."

4. Letter of October 17, 1985, from Klaus L. Stemmer, M.D. to Monsanto.

"In your letter of September 17, 1985, you requested an evaluation of the material, submitted with the letter, of the mouse kidney tumor data found in the chronic feeding study of glyphosate. In addition, I received the kidney sections of the male and female mice of this experiment."

"I reviewed the kidney slides of the male mice and confirmed the findings of renal tubular neoplasms in the following five (5) animals: 1028, 3023, 4029, 4032, and 4041. These tumors were cytologically well differentiated. I could not verify any pre-malignant features in the renal tubular epithelium of any of the experimental mice. Intercurrent renal diseases, which were noticed, did not support any cytotoxic effect of the test material. Also, no histologic changes were present suggesting that the test material might enhance carcinogenesis."

"The final report furnished by Bio/dynamics Inc. on July 21, 1983, does not enumerate any pathologic alterations in the kidneys of the male mice that could be interpreted as enhancement of the development of neoplasms (pages P1 to P17 of report). I am certain that the pathologists examined the kidneys for lesions of that nature since they did and reported them for the liver. The lack of finding such changes supports the statement in the previous paragraph and in the report of M. Kuschner, M.D."

"The historical data on the incidence of renal tubular adenomas were reviewed. Bio/dynamics Inc. reported a percentage range from 0 to 3.3 percent; International Research and Development Corporation found a percentage range from 1 to 2 percent, and Hazelton had a range from 0 to 3.6 percent. In the present chronic feeding study, the incidence in control male mice was 2 percent. As is stated in the Hazelton report, the expected percentage incidence could be as high as 7 percent. On the basis of these data, the occurrence of three renal tubular adenomas in the high dose group (6%) would still fall into the general percentage range of male control CD-1 mice."

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"The data in appendices 17 A and 17 B strongly indicate that the CD-1 mouse has a high incidental occurrence of neoplasms in many different organs (report of Bio/dynamics Inc.). The incidence is: control 20 out of 50 mice, low dose 28 out of 50, medium dose 29 out of 50, and high dose 24 out of 50. In evaluating the potential tumorgenicity or carcinogenicity of the test compound one should take this into consideration. It might be that one can find a slight statistical significance in the "dose related" data, if one ignores the historical data (previous paragraph). Whether this has any biological significance is doubtful. In the CD-1 mouse having a high occurrence of neoplasms, the "dose related" incidence of renal tubular adenomas is in all probability biologically by chance."

5. Letter of October 10, 1985, from Pathology Working Group (PWG) to Monsanto.

Participants in the PWG

Dr. R. M. Sauer (Chairperson)
Dr. M. R. Anver
Dr. J. D. Strandberg
Dr. J. M. Ward
Dr. D. G. Goodman

Conduct of the PWG Review

"Prior to the PWG review, the Chairperson reviewed the pathology incidence tables, the original pathologist's (OP) narrative, pertinent individual animal records and all tissue sections of kidneys from male mice. The letter included the original set of kidney sections which were read both by the OP and Dr. Kuschner and a subsequently prepared set of 3 step sections from each kidney block which had been read by the OP. The kidney was the designated target organ for the PWG review."

"The PWG blindly examined coded slides without respect to treatment group of all cases or renal tubular-cell tumors and all discrepancies in diagnoses among the OP, Dr. Kuschner and the Chairperson of renal tubular-cell tumors and renal tubular-cell hyperplasias. The consensus viewpoint of the participants is recorded in Appendix A."

"The PWG also reviewed all sections of kidneys from control and high dose males for incidence and severity of naturally occurring conditions and induced toxic lesions."

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Comments and Recommendation of the PWG

"Microscopically, tubular cell adenomas are well circumscribed and compress the adjacent parenchyma. They are composed of variably sized cuboidal, columnar or polygonal cells which form solid lobules separated by delicate connective tissue septa. The cytoplasm may be basophilic but is usually eosinophilic and granular or vaculated and reticular. The nuclei are round and open faced. Mitoses are infrequent."

"Tubular-cell carcinomas are usually larger and may invade the adjacent parenchyma. The cells are more pleomorphic than in the adenomas and often contain large bizarre nuclei. Mitoses, while not common, are more frequent than in adenomas. Necrosis, hemorrhage and cholesterol clefts are often present."

"Renal tubular-cell hyperplasia consists of a small circumscribed lesion with or without increased basophilia and an increased number ~~of~~ nuclei piling up and filling the lumen. There is usually some expansion of the tubule and loss of tubular architecture but without compression of adjacent parenchyma. Typically the cells have poorly defined cytoplasmic borders, round open-faced nuclei and have a relatively high nuclear/cytoplasmic ratio."

"The incidence of renal tubular-cell neoplasms as determined by the PWG is presented in Table I. Because differentiation between tubular-cell adenoma and tubular-cell carcinoma is not always clearly apparent and because both lesions are derived from the same cell type it is appropriate to combine the incidences for purposes of evaluation and statistical analysis."

TABLE I
RENAL TUBULAR-CELL LESIONS

	Male Mice			
	Control	Low Dose	Medium Dose	High Dose
Tubular-cell adenoma	1	0	0	1
Tubular-cell carcinoma	0	0	1	2
Combined incidence	1	0	1	3

"This PWG firmly believes and unanimously concurs with the original pathologist and reviewing pathologist that the incidences of renal tubular-cell neoplasms in this study are not compound related."

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"The following points were taken into consideration in reaching this decision:"

"a) Renal tubular-cell tumors are spontaneous lesions for which there is a paucity of historical control data for this mouse stock. However, clustering can occur and the incidence in this study is comparable to the available historical control range from several laboratories (Appendix B). Since there were 3 treated groups and only 1 control group, there is a greater possibility of more variation from mean control incidences in the treated mice."

"b) None of the treatment groups differed from the controls by the Fisher exact test at the 0.05 level of significance. Over all groups there was no evidence of a significant linear trend at the 0.05 level by a one-tailed Cochran-Armitage Test."

"c) Multiple renal tumors were not found in any animal."

"d) Compound related nephrotoxic lesions, including preneoplastic changes, were not present in this study. In addition, renal toxicity was not noted in the 3-month subchronic toxicity study reported in December 1979."

"Spontaneous chronic renal disease is commonly seen in aged mice. It consists of a spectrum of lesions which may occur individually or in various combinations in any particular kidney. Individual lesions reported by the OP in this study and listed in his updated report may be components of this complex. Chronic interstitial nephritis, a term used by the OP, is a summary and redundant diagnosis which encompasses several of the individual components and should not be singled out for statistical analysis."

"Many animals in this study had proliferative, cystic lesions of the parietal layer of Bowman's capsule and of the proximal convoluted tubules. These changes were apparently more severe in control than treated animals."

"Based on the review of all high dose and control male kidneys, the PWG did not observe an increase in incidence or severity of non-neoplastic lesions in the kidney of high dose animals. The PWG concurs with the OP that there is no evidence that these lesions were compound induced or related."

Appendix E: EPA Redacted example

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

NOV 25 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Glyphosate - Possible 6 (a)(2) Effect in 2-Generation Rat Reproduction Study Submitted by Monsanto in Letter of November 15, 1989

Caswell No.: 661A
HED Project No.: 0-0504
Record No.: 257892

FROM: William Dykstra, Ph. D.
Review Section I
Toxicology Branch I
Health Effects Division (H7509C)

William Dykstra 11/20/91

THRU: Roger Gardner, Section Head
Review Section I
Toxicology Branch I
Health Effects Division (H7509C)

Roger Gardner 11/20/91

TO: Robert J. Taylor, Product Manager 25
Registration Division (H7507C)

Requested Action

Review possible adverse effects [6(a)(2) data] reported by Monsanto from the 2-generation rat reproduction study.

Recommendations and Conclusions

The results reported by Monsanto in their letter of November 15, 1989, do not suggest an adverse reproductive effect under FIFRA 6(a)(2) (Reporting Code 9, 40 CFR, 158.34).

Background

In a letter dated November 15, 1989, the Registrant (Monsanto) described results from a multigeneration reproduction study in rats as follows:

> ...Groups of 30 male and 30 female Sprague-Dawley rats were administered glyphosate through their diet at concentrations of 0, 2000, 10,000, and 30,000 ppm. The F_0 adults produced one litter of animals and the F_1 adults produced two successive litters...

There were statistically significant reductions (relative to controls) in body weights of high dose (30,000 ppm) group adults. Similar body weight reductions (statistically significant) were noted in pups of the high dose group on lactation days 14 and 21. Smaller decreases were noted in some mid dose (10,000 ppm) pups but only on lactation day 21. There was a slight but statistically significant decrease in the number of F_1 pups per litter at birth in the high dose group. No statistically significant decrease was noted in the F_{2A} or F_{2B} litters but a slight treatment-related effect cannot be ruled out at the high dose. There were no treatment-related effects at the low dose (2000 ppm) animals. These results are preliminary and have not been fully evaluated.

Comments

The reference dose (RfD) for glyphosate was based on a previous 3-generation reproduction study with a no-observed-effect level (NOEL) of 10 mg/kg/day, and the RfD is 0.1 mg/kg/day based on the NOEL and an uncertainty factor of 100. If the effects reported at the mid dose level of 10,000 ppm (500 mg/kg/day) can be attributed to the administration of glyphosate, the NOEL of 2000 ppm (100 mg/kg/day) is 1000 times the existing RfD (ADI). Therefore, the reported information did not suggest that glyphosate meets the criterion for 6(a)(2) adverse reproductive effects data (40 CFR, 158.34, Reporting Code 9).

According to the PDMS, the study described in the November 15 letter has been submitted to the Agency and has the following listing:

MRID 41621501. Reyna, M. (1990) Two Generation Reproduction Feeding Study with Glyphosate in Sprague Dawley Rats: Lab Project No. MSL-10387. Unpublished study prepared by Monsanto Agricultural Co. 1158 p.

This study was received by the Agency on September 6, 1990, and has not been forwarded to Toxicology Branch I for review as of the date of this memorandum.

2

GLYPHOSATE 103601

Page____ is not included in this copy.

Pages 3 through 4 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

X MONSANTO CLAIMS CONFIDENTIAL

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

DATE OUT: _____

SUBJECT: PRODUCT CHEMISTRY REVIEW OF MP [ ] EP [X]
DP BARCODE No.:D226250 REG./File Symbol No.: 524-UOG
PRODUCT NAME: MON 58420 Herbicide

DATE: September 12, 1996

TO: Robert Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division(7505C)

FROM: Shyam B. Mathur, Ph.D., Chemist
Product Chemistry Review Section
Registration Support Branch/RD (7505W)

THRU: Harold Podall, Ph.D., Section Head
Product Chemistry Review Section
Registration Support Branch/RD(7505W)

SBMathur 9-17-96

HP 9/18/96

SUMMARY OF FINDINGS

1. The basic formulation CSF(dated April 15, 1996) is filled out correctly and completely in compliance with PR Notice 91-2 and agree with the label claim nominal concentration.[61-1 & 62-2].
2. The data submitted corresponding to guideline reference 61-2 and 61-3 satisfy the data requirements of 40CFR§158.165 and 158.167 respectively.
3. The data submitted corresponding to guideline reference 62-1 and 62-3 satisfy the data requirements of 40CFR§158.170 and 158.180 respectively.
4. The data submitted corresponding to guideline reference 63-3,7, 12,14-16,18, & 21 satisfy the data requirements of 40CFR §158.190. The registrant informed that the studies on storage stability(63-17) and corrosion characteristics will be initiated this year(1996).
5. The registrant carried out analysis for following nitrosamines: N-nitrosoglyphosate(NNG), N-nitrososarcosine(NNSAR), N-nitroso-methylaminomethyl phosphonic acid(NNMAMPA), N-nitrosoiminodi-acetic acid(NNIDA), and N-nitrosoimino-bis-methylene-bis-phos-phonic acid(NNTB). Out of all these nitrosamines, only N-nitroso glyphosate(NNG)was detected in less than 1 ppm.

Note to PM:

a. The acetochlor [redacted] has been shown to be [redacted] in REFS, whereas the registrant in CSF indicated it to be [redacted]
b. N-Phosphonomethylglycine, MON 0139 isopropylamine salt [redacted] has been shown to be [redacted] in REFS, whereas the registrant in the CSF indicated it to be [redacted]

7505W:RD:RSB:PCRS:CS-1:Rmxxx:Reviewer:S.B.MATHUR:09/12/96:703-308-8378:Code No.(Reg. No 524-UOG). <PCFORM>

PRODUCT INGREDIENT SOURCE INFORMATION IS NOT INCLUDED

PRODUCT CHEMISTRY REVIEW OF MP [ ] EP [X]
DP BARCODE No.:D226250 REG./File Symbol No.: 524-UOG
PRODUCT NAME: MON 58420 Herbicide
DATE: September 12, 1996

1. Reviewer: S.B.Mathur 2. Company: Monsanto Agriculture Co.

3. Type of Submission: Registration [X] Reregistration [ ]
New [X] Resubmission [ ] Amendment [ ] "ME-TOO" [ ]
Alternate Formulation [ ] Experimental Use Permit [ ]
Other (Specify)_____

4. If "Me-TOO" Registration, this product is [ ] is not [ ] similar or substantially similar to EPA's Reg. No.:_____

If not, comment in Confidential Appendix A on the differences between the registered and the new source where significant.

CONFIDENTIAL STATEMENT OF FORMULA

5. Type of formulation and the sources of active ingredients:

• Non-integrated formulation system.....[X]
• Are all technical grade active ingredients used registered?
• yes [ ] • no [ ], If no, specify _____

• Integrated formulation system.....[ ]

6. Clearance of intentionally added ingredients in the formulation for the intended use (indicate in the Confidential Appendix those that are not cleared; the PC Codes should be provided by the chemist on the CSF for those that are cleared):

6(a) Formulation intended for food use under 40CFR§180.1001:
• yes [X] • no [ ] • Some are cleared, others are not [ ]
Cleared under list: • c[X] • d[X] • e [X]
Are there any limitations for use as an inert under 40CFR§180.1001?
• yes [ ] • no [ ], If yes, specify _____

6(b) Formulation intended for non-food use:
• yes [ ] • no [X] • Some are cleared, others are not [ ]

6(c) Clearance by the FDA of certain formulations under 21CFR§170 to 199. Examples: (a) indirect food additives, such as food contact surface sanitizers; adhesives, coatings, paper and paperboard products that may contact food in packaging or holding; and (b) substances generally recognized as safe (GRAS).
• yes [ ] • no [ ] • Some are cleared, others are not [ ]
If yes, the entire formulation is cleared under 21CFR§_____.

PRODUCT (INGREDIENT SOURCE INFORMATION IS NOT INCLUDED)

7. The density, pH, and flammability values given on the CSF are identical with those of GRN 63-7, 63-12, and 63-15, respectively: • yes [X] • no [ ]

8. The nominal concentrations (NC) of the active ingredients and the upper and lower certified limits (UCL & LCL) are as follows:

Active ingredient(s)	% by weight NC	UCL	LCL
Acetochlor	[redacted]	(21.50)	
MON 0139 Isopropyl amine salt	[redacted]	(8.10)	
[redacted] Atrazine	[redacted]	(16.10)	

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

9. The calculated NCs, based on the pure active ingredients (PAI), are identical to those on the label:
• yes [X] • no [ ]

10. The certified limits are within the standard limits as per 40CFR§158.175 or are adequately explained if different:
• yes [X] • no [ ]

PRODUCT LABEL

11. The chemical names of the active ingredients on the label are identical to those on the CSF: • yes [X] • no [ ]

12. The appropriate physical and chemical hazards statement regarding flammability or explosive characteristics of the product are given on the label:
• yes [ ] • no [ ] • not applicable [X]

13. The storage and disposal instructions for the pesticide and container are in compliance with PR Notice 84-1 for household use products or PR Notice 83-3 for all other uses:
• yes [X] • no [ ]

4

PRODUCT CHEMISTRY DATA (SERIES 61, 62, 63)

14. Chemical IDs/Manufacture/ Analytical Information		Data Required Fulfilled	MRID No.
61-1	Chemical Identity(CSF)	Y	04-15-96
61-2	Start.Mat.& Mfg.Process	Y	440004-01
61-3	Discussion of Impurities	Y	" "
62-1	Preliminary Analysis	Y	" "
62-2	Certified Limits(CSF)	Y	04-15-96
62-3	Enforcement Analytical Method	Y	440004-01

15. Physical/Chemical Properties		Data Required Fulfilled	Value or Qualitat. Descrip.	MRID No.
63-3	Physical State	Y	Liquid	" "
63-7	Density/Bulk Density	Y	9.3 lbs per gal.	" "
63-12	pH of Product	Y	5.48	" "
63-14	Oxid/Red Action	Y	Note 1	" "
63-15a	Flamma.-Flsh.Pt.	Y	>210°F	" "
63-15b	Flame Extension	NA		
63-16	Explodability	Y	None	" "
63-17	Storage Stability	I	Note 2	" "
63-18	Viscosity	Y	682 cPs at 30 RPM	" "
63-19	Miscibility	NA		
63-20	Corros.Charact.	I	Note 2	" "
63-21	Dielec.Bkd.Vltg.	NA		

Explanations: Y = The Requirements Were Fulfilled; N = The Requirements Were Not Fulfilled; NA = Not Applicable; G = Data Gap; U = Requires Upgrading; I = Incomplete or In Progress; W = Waived.
Note 1. 63-14. Oxi./Red. Property: The reagents were added to the EP in a mass ratio 5:1 of EP to the reagent. The reagents used were water, Zn, $NH_4H_2PO_4$, and 1% $KMnO_4$. The product was oxidized by 1% $KMnO_4$.
Note 2. 63-17 and 63-20.: the registrant reported that these two studies will be initiated together in 1996.

4

Product Chemistry Review for 524-493 dated 9/18/96

Page ____ is not included in this copy.

Pages 5 through 8 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

X The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

organisms in neighboring areas. Do not contaminate water when disposing of equipment washwater.

This chemical demonstrates the properties and characteristics associated with chemicals detected in ground water. The use of this chemical in areas where soils are permeable, particularly where the ground water is shallow, may result in ground water contamination.

Acetochlor has properties that may result in surface water contamination via dissolved runoff and erosion. Practices should be followed to minimize the potential for dissolved runoff and/or runoff erosion.

Physical or Chemical Hazards

Spray solution of this product should be mixed, stored and applied only in stainless steel, aluminum, fiberglass, plastic and plastic-lined steel containers.

DO NOT MIX, STORE OR APPLY THIS THIS PRODUCT OR SPRAY SOLUTIONS OF THIS PRODUCT IN GALVANIZED STEEL OR UNLINED STEEL (EXCEPT STAINLESS STEEL) CONTAINERS OR SPRAY TANKS. This product or spray solutions of this product react with such containers and tanks to produce hydrogen gas which may form a highly combustible gas mixture. This gas mixture could flash or explode, causing serious personal injury, if ignited by open flames, sparks, welder's torch, lighted cigarette or other ignition sources.

ACTIVE INGREDIENTS:*	
Acetochlor,[2-chloro-N-ethoxymethyl-N-(2-ethyl-6-methylphenyl)acetamide]	21.5%
Atrazine, [2-chloro-4-(ethylamino)-6-(isopropylamino)s-triazine] and related triazines	16.1%
Glyphosate,[N-phosphonomethyl)glycine, in the form of its isopropylamine salt	8.1%
INERT INGREDIENTS:	54.3%
	100.0%

*Contains 240 grams/liter or 2.0 pounds/gallon of acetochlor, 180 grams/liter or 1.5 pounds/gallon of atrazine and related compounds and 90 grams/liter or 0.75 pound/gallon of glyphosate, in the form of its isopropylamine salt which is equivalent to 0.56 pounds/gallon of the acid, glyphosate.

This product is protected by U.S. Pat. No. 4,256,481 and U.S. Patent No. 4,405,531. Other patents pending. No license is granted under any non-U.S. patent(s)

Appendix F: GAO Redacted Example

096904

76-60096

REPORT TO THE CONGRESS

BY THE COMPTROLLER GENERAL OF THE UNITED STATES

Federal Pesticide Registration Program: Is It Protecting The Public And The Environment Adequately From Pesticide Hazards?

Environmental Protection Agency

Food And Drug Administration (HEW)

GAO found the following conditions:

Safety and efficacy data has not been submitted to support marketing many pesticides. (Safety data include information on cancer, genetic changes, birth defects, and reproduction.)

--Safety and efficacy data is not required for the pesticides as marketed, only for individual active ingredients.

--Reviews of inert ingredients (such as vinyl chloride) are not subjected to the full range of safety testing.

--Many labels do not comply with requirements.

--Pesticide residue tolerances are not monitored or reviewed.

--The safety of pesticide residues in some foods has not been determined.

--Statutory registration requirements are not carried out on a timely basis.

REC-76-42

Appendix G: Toxicity Chart

Toxicity Chart

ACUTE ORAL TOXICITY:	**ACUTE ORAL TOXICITY:**
Category I $LD_{50} \leq$ 50 mg/kg DANGER Skull and Crossbones Fatal if swallowed	**Category 1** $LD_{50} \leq 5$ mg/kg ***and*** **Category 2** $LD_{50} > 5$ mg/kg ≤ 50 mg/kg DANGER Skull and Crossbones in diamond Fatal if swallowed
Category II $LD_{50} > 50$ mg/kg ≤ 500 mg/kg WARNING No symbol May be fatal if swallowed	**Category 3** $LD_{50} > 50$ mg/kg ≤ 300 mg/kg DANGER Skull and Crossbones in diamond Toxic if swallowed **Category 4** $LD_{50} > 300$ mg/kg ≤ 2000 mg/kg WARNING Exclamation point in diamond Harmful if swallowed
Category III $LD_{50} > 500$ mg/kg ≤ 5000 mg/kg CAUTION No symbol Harmful if swallowed	**Category 5** $LD_{50} > 2000$ mg/kg ≤ 5000 mg/kg (See Note (*e)* to GHS Table 3.1.1.) WARNING No symbol May be harmful if swallowed
Category IV $LD_{50} > 5000$ mg/kg CAUTION or no signal word No symbol No hazard statement required; registrant may choose to use Category III statement	[$LD_{50} > 5000$ mg/kg not classified; no specified label elements]

Appendix H: USDA-EPA Scientists Statement

Anonymous public comment

Document ID: EPA-HQ-OPP-2008-0836-0043
This is comment on PROPOSED RULE: FIFRA Scientific Advisory Panel; Notice of Public Meeting
Docket ID:EPA-HQ-OPP-2008-0836

The following statement has been submitted by 26 leading corn insect scientists working at public research institutions located in 16 corn producing states. All of the scientists have been active participants of the Regional Research Projects NCCC-46 "Development, Optimization, and Delivery of Management Strategies for Corn Rootworms and Other Below-ground Insect Pests of Maize" and/or related projects with corn insect pests. The statement may be applicable to all EPA decisions on PIPs, not just for the current SAP. It should not be interpreted that the actions and opinions of these 26 scientists represent those of the entire group of scientists participating in NCCC-46. The names of the scientists have been withheld from the public docket because virtually all of us require cooperation from industry at some level to conduct our research.

Statement: "Technology/stewardship agreements required for the purchase of genetically modified seed explicitly prohibit research. These agreements inhibit public scientists from pursuing their mandated role on behalf of the public good unless the research is approved by industry. As a result of restricted access, no truly independent research can be legally conducted on many critical questions regarding the technology, its performance, its management implications, IRM, and its interactions with insect biology. Consequently, data flowing to an EPA Scientific Advisory Panel from the public sector is unduly limited."

Appendix I: NK603 European Regulations

In 2004, EU approved NK603 for food/feed market (but not for cultivation). The final approval, by the European Commission takes into consideration:

- The European Parliament and Council of 12 March 2001 Directive 2001/18/EC (on the deliberate release into the environment of genetically modified organisms)
- The EFSA's authority, requirements and procedures regarding food law and safety according to EC 178/2002
- EC suggests that EC 1830/2003 (regarding labeling) be used to help streamline market transactions as well as secure necessary product information in case of health hazard recall. Within this regulation, 1829/2003 (on genetically modified food and feed) was referred to regarding keeping track of products registered as GMO or containing GMOs. 1829/2003 was also directly mentioned in Article 1: Consent.
- This regulation states that it grants authority to CA in Spain to place NK603 on the market without prejudice to EC 258/97 (concerning novel food and novel food ingredients, but this regulation was REPEALED and replaced with EC 2015/2283 (on novel foods)—which also replaces EC 1852/2001 (on laying down detailed rules for making certain information available to the public and for the protection of information pursuant to European Parliament and Council Regulation EC 258/9) and amends EC 1169/2011 (on the provision of food information to consumers**)** . Cited in EC 258/97 (which pertains to NK603) is:

Directive 70/457 of 29 September 1970 on the common catalogue of varieties of agricultural plant species (REPEALED in 2002 and replaced with EC 53/2002 on the common catalogue of varieties of agricultural plant species…which mainly covers seeds/cultivation crops, so it doesn't apply to NK603);

Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms (for establishing a Community system for environmental assessment. (REPEALED and replace with EC 2001/18);

EC 258/97 suggests that public health concerns be addressed to Scientific Committee for Food set up by Decision 74/234/EEC (this committee was absorbed into the EFSA in 2003);

states that Directive 89/397/EEC of 14 June 1989 on the official control of foodstuffs (REPEALED and replace by EC 882/2004 on official controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules) and Council Directive 93/99/EEC of 29 October 1993 on the subject of additional measures concerning the official control of foodstuffs apply to novel foods or food ingredients (REPEALED in 1993 and replaced with 93/10 EEC establishing implementing provisions for Council Decision 92/481/EEC on the adoption of an action plan for the exchange between Member State administrations of national officials who are engaged in the

implementation of Community legislation required to achieve the internal market (Karolus Programme), which was amended in 1994 by EC 94/818 (same title);

69/414/EEC on setting up a Standing Committee for Foodstuffs (REPEALED in 2002 and replaced with EC 178/2002 on laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety);