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Regulating in Uncertainty: Animating the Public Health Product Safety Net to Capture Consumer Products Regulated by the FDA that Use Innovative Technologies, Including Nanotechnologies, Genetic Modification, Cloning, and Lab Grown Meat

Katharine Van Tassel[†]

I. INTRODUCTION

“For want of a nail, the war was lost.”¹

The past several decades have seen the creation of transformative new technologies that are being used to design

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¹ Part of a proverbial rhyme showing that small actions can result in large consequences:

For want of a nail the shoe was lost.

For want of a shoe the horse was lost.

For want of a horse the rider was lost.

For want of a rider the message was lost.

For want of a message the battle was lost.

For want of a battle the kingdom was lost.

And all for the want of a horseshoe nail.

Benjamin Franklin, *Poor Richard's Almanack* 69 (1758). This Article will explain how the powerful public health product safety net is activated when innovative ingredients are identified on product labels. For example, nanotech ingredients can be identified with just four simple letters, “nano,” in front of each ingredient that is nano-sized, or just two letters, “GM,” can be placed in front of ingredients that are genetically modified. With just the simple step of placing a couple of letters on the ingredient lists on product labels, the public health product safety net will be activated, potentially averting a public health crisis from exposures to novel, innovative ingredients. Thus, this small action could avert a large consequence.

innovative consumer product ingredients never before seen in nature. Examples include the use of nanotechnology and genetic modification, and, right around the corner, cloned animals used for food, as well as lab-grown meat.² These innovative, novel³ technologies are harbingers of more pioneering consumer product ingredients to come. This remarkable pace in the development of groundbreaking new technologies means that the population is being steadily exposed to novel ingredients with unknown health risks.

Optimally, the Food and Drug Administration (FDA) should be regulating these innovative, novel ingredients in consumer products to meet the twin goals of fostering innovation while protecting public health. However, the current litmus test that the FDA is using to trigger regulation to protect public health is focused on *hazard*.⁴ Linking public health protections to the degree of hazard when operating in scientific uncertainty is outcome determinative—it means no regulation to protect public health at all. This is because it is common for the development of innovative, novel technologies to far outpace the development of the science necessary to test for the health risks associated with these technologies.⁵ This scientific lag time creates an information void with regard to risks to human health that can

² See generally Henry Fountain, *Building a \$350,000 Burger*, NY Times (May 12, 2013), online at http://www.nytimes.com/2013/05/14/science/engineering-the-325000-in-vitro-burger.html?pagewanted=all&_r=0 (visited Sept 15, 2013) (describing a five ounce hamburger being assembled from tiny bits of lab grown beef muscle tissue in a lab that will be eaten at an event at London to show the world that lab grown meat is possible); Zachary Schneider, Comment, *In Vitro Meat: Space Travel, Cannibalism, and Federal Regulation*, 50 Houston L Rev 991 (2013) (describing why lab grown meat could ease many of the environmental burdens of worldwide meat production).

³ These products are described as both innovative and novel. In technology, an innovation “may be an improvement to something already existing.” Merriam-Webster, “Innovation” (Merriam-Webster 2013), online at <http://www.merriam-webster.com/dictionary/innovation> (visited Sept 15, 2013). On the other hand, to be “novel” means “new and not resembling something formerly known or used.” Merriam-Webster, (Merriam-Webster 2013), online at <http://www.merriam-webster.com/dictionary/novel> (visited Sept 15, 2013). Thus, the descriptive “novel innovation” as used in this Article means an improvement to an already existing product that involves the use of ingredients that are new and that do not resemble anything formerly used or known. Examples include nanotech particles, GM food, cloned animals used as food, or lab-grown meat.

⁴ See notes 95–109 and accompanying text.

⁵ For a series of examples dealing with tributyltin (“TBT”), polychlorinated biphenyls (“PCBs”), diethylstilbestrol (“DES”), the Great Lakes pollution, thalidomide, medical x-rays, benzene, asbestos, chlorofluorocarbons (“CFCs”), and DES, see Part II.E.1.

last for decades.⁶ This health risk information void cripples the FDA's ability to regulate to protect public health during this often decades-long period of scientific uncertainty.⁷

Many propose that the proper way to deal with the problems caused by this health risk information void is to adopt some form of the Precautionary Principle. According to Professor Cass Sunstein, “[s]imply put, the principle counsels that we should avoid steps that will create a risk of harm; until safety is established through clear evidence, we should be cautious. In a catch-phrase: Better safe than sorry.”⁸ However, there are downsides to this approach. Professor Sunstein points out that the bar to the use of innovative technologies for the time period it takes to prove them to be safe comes with its own harm—keeping the potentially life-saving benefits of these innovative technologies from reaching people in need.⁹ Professor Sunstein gives the example of genetically modified food (“GM food”), which may allow the production of food that is healthier, cheaper, and easier to grow under difficult environmental conditions.¹⁰ This GM food may provide great benefits to the populations of developing countries, including the prevention of many deaths.¹¹ Following the Precautionary Principle means refusing to allow the use of GM food until it is proven to be safe.

⁶ See notes 112–121 and accompanying text.

⁷ See notes 122–134 and accompanying text.

⁸ Cass R. Sunstein, *The Paralyzing Principle*, 25 Reg 32, 32 (2003). Professor Sunstein explains that the Precautionary Principle has a wide range of definitions, from weak to strong. An example of what he refers to as a weak version is that which was adopted by the 1992 Rio Declaration that states “[w]here there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.” *Id.* at 33. An example of a strong version of the Precautionary Principle that Professor Sunstein uses is drawn from the

widely publicized Wingspread Declaration, from a meeting of environmentalists in 1998 . . . “When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not established scientifically. In this context, the proponent of the activity, rather than the public, should bear the burden of proof.”

Id.

⁹ *Id.*

¹⁰ *Id.*

¹¹ Professor Sunstein clarifies that “the point is not that genetic modification will definitely have those benefits, or that the benefits of genetic modification outweigh the risks. The point is only that if the Precautionary Principle is taken literally, it is offended by regulation and by non-regulation.” *Id.*

This means that the potential benefits of GM food will be withheld during the health risk information void. Thus, this choice brings its own risks of harm.

How should the FDA regulate consumer products to protect public health when operating in scientific uncertainty? This Article suggests that, when it comes *individual risk*,¹² such as those risks faced by individual consumers when choosing and using a particular product—in contrast to *collective risks* such as those environmental risks faced by all individuals as a collective¹³—neither of these “all or nothing” approaches fits the bill.

This Article is the first to propose a unique, yet entirely feasible, middle ground that uses what this Article calls the public health product safety net. Instead of a focus on the unknown, which is the degree of hazard associated with a new and innovative technology, the lodestar of the FDA for regulation in the context of consumer products should be on *novelty*.¹⁴ Keying regulation to novelty allows for “strings” to be attached to consumer products using novel technologies. These strings take the form of a requirement that all ingredients created through the use of novel technologies be listed in the ingredient section of product labels. This requirement allows for data collection and tracking to ensure that, if an innovative technology is, in fact, harmful, public health officials can identify this fact relatively quickly, pull the attached “strings” to rapidly recall the consumer product, and avert, or at least mitigate, a possible public health disaster. This Article describes how a focus on novelty, coupled with an already-existing provision in the Food, Drug, and Cosmetic Act (FDCA, or “the Act”) requiring that all material information be provided on product labels, triggers an ingredient-listing requirement.

Importantly, ingredient listing is the key to the public health product safety net.¹⁵ In a nutshell, novel ingredient

¹² For a discussion of the difference between *individual risk* and *collective risk* and what this difference means to appropriate regulatory choices, see notes 189–193 and accompanying text.

¹³ *Id.* Of note is that these approaches are also problematic when dealing with collective risk. This topic is beyond the scope of this Article as the issues relating to collective risk are, in many ways, very different from those arising in the context of individual risks, including the appropriate role of government.

¹⁴ See notes 189–195 and accompanying text.

¹⁵ This term is different from what the popular literature refers to as the *health*

listing protects consumer safety through consumer self-protection. If a consumer knows that she is being exposed to a novel ingredient, she can use heightened vigilance for symptoms of harm. It also allows for the appropriate treatment of injured consumers by medical professionals who will, for the first time, be able to identify novel ingredients as potential causative agents through accurate exposure reporting by consumers. Ingredient listing also allows for the proper reporting of injury-causing agents to state and federal public health protection agencies in charge of the early warning and product recall systems. Finally, the data collected by these public health protection agencies provides the evidence needed to actuate the instrumental use of the tort system to encourage the proper investment in product safety and to insulate against the overuse and overconsumption of relatively risky products. Together, these public and private actors join to form the public health product safety net.¹⁶

While this system is far from perfect, it is likely to improve exponentially as this country moves into the era of big data.¹⁷ The public health product safety net will use big data strategies to take more traditionally created data generated by the state and federal consumer product reporting systems and link it to the information that is only recently being gathered from a massive collection of electronic health records.¹⁸ Adding to this

care safety net that refers to health care providers who provide care to low-income people. See, for example, Coalition of Community Health Clinics, *What is the Health Care Safety Net*, online at <http://www.coalitionclinics.org/safety-net.html> (visited Sept 15, 2013) (“Health care safety net clinics are community-based providers who offer health services to low-income people, including those without insurance.”).

¹⁶ See notes 175–184 and accompanying text.

¹⁷ See *Data, data everywhere*, *The Economist* (Feb 25, 2010), online at <http://www.economist.com/node/15557443> (visited Sept 15, 2013) (“[T]he world contains an unimaginably vast amount of digital information which is getting ever vaster ever more rapidly. This makes it possible to do many things that previously could not be done: spot business trends, prevent diseases, combat crime and so on. Managed well, the data can be used to unlock new sources of economic value, provide fresh insights into science and hold governments to account.”); Dan Kusnetzky, *What is “Big Data”?*, *Virtually Speaking* (ZDNet Feb 26, 2010), online at <http://www.zdnet.com/blog/virtualization/what-is-big-data/1708> (visited Sept 15, 2013) (“In simplest terms, the phrase refers to the tools, processes and procedures allowing an organization to create, manipulate, and manage very large data sets and storage facilities.”).

¹⁸ Thomas L. Friedman, *Obamacare’s Other Surprise*, *NY Times* (May 25, 2013), online at <http://www.nytimes.com/2013/05/26/opinion/sunday/friedman-obamacares-other-surprise.html?emc=tnt&tntemail0=y> (visited Sept 15, 2013) (detailing the remarkable growth in conversion to electronic medical records and the use of data mining to access information contained therein).

data stream is an enormous amount of new information that is being culled through the 2013 phenomenon of data mining, consumer use of social media, such as tweets and on-line discussion forums, as well as search engines such as those created by Google, Microsoft, and Yahoo, in order to identify defective products that cause physical harm. Just this year, scientists announced that they were able to use the data from these unique sources to identify harmful product defects significantly before the FDA,¹⁹ and several apps have been developed to track food-borne illnesses using data collected from Twitter.²⁰ All told, these integrated data streams will ultimately create a highly sensitive, state-of-the-art, consumer product safety surveillance system.²¹ This system will identify early warnings of product safety problems associated with ingredients created by innovative technologies to proactively mitigate their effects through national product warning notifications and recalls.

Adding to this picture, a focus on novelty fits well with the overarching theme of the FDCA that titers the degree and kind of regulation it uses to protect consumers from harm from third parties to the level and type of vulnerability of those consumers. It also tracks how the Act has historically dealt with regulating novel ingredients when the health risks associated with these ingredients are unknown.²²

Finally, the result of this focus on novelty reflects the appropriate role of the government when protecting its citizens against the risks of harm by third parties. In the context of consumer products and individual risk, the proper role of the government is to protect individual choice with regard to the amount and nature of the risk the consumer is willing to encounter. This contrasts with the appropriate role of government in the context of collective risk created by third

¹⁹ See notes 122–124 and accompanying text.

²⁰ Beth Krietsch, *Social Media Apps Use Twitter to Track Illness Outbreaks*, Food Safety News (Aug 19, 2013), online at <http://www.foodsafetynews.com/2013/08/social-media-moves-to-help-detect-outbreaks/> (visited Sept 15, 2013); *Tracking Twitter May Enhance Monitoring of Food Safety at Restaurants*, ScienceDaily (Aug 7, 2013), online at <http://www.sciencedaily.com/releases/2013/08/130807134510.htm> (visited Sept 15, 2013).

²¹ See note 20.

²² See notes 135–175 and accompanying text.

parties when the individual has no ability to avoid the risk through their own means.²³

This Article will use nanotechnology as an example that highlights how regulation based on *novelty* rather than *hazard* achieves the proper balance between protecting public health while encouraging innovation through the animation of the public health product safety net. In Part II, this Article starts by explaining what nanotechnology is and the remarkable growth of its use in everyday consumer products. It then summarizes the steadily increasing number of studies that suggest that there are likely to be serious health risks associated with the use of nanotech consumer products. Next, it explains how the FDA is currently regulating these products by focusing on the degree of hazard and the serious problems that arise from this misguided focus. In Part III, the history of the FDCA is summarized in order to explain how, and why, the FDCA came to titer the degree and kind of regulation it uses to protect consumers from harm from third parties to the level and type of vulnerability of targeted consumers. Next, this Article builds on this history to describe how the Act has historically dealt specifically with regulating novel ingredients with unknown health risks in order to deal with consumer vulnerabilities. This history is then used to illuminate the reasons why a switch from a focus on *hazard* to a focus on *novelty* is supported by precedent and better fits the policies and goals of the FDCA while, at the same time, achieving the proper balance between protecting public health and encouraging innovation. This Article shows how a simple provision that is already a part of the FDCA can be relied upon to require ingredient listing based on novelty so that additional legislation is not required. In Part IV, this Article illustrates how this focus will operate to achieve the balance between safety and innovation with other innovative, novel technologies used as ingredients in consumer products such as cloned animals, genetically modified plants and animals used for food, as well as with lab-grown meat. Finally, in Part V, this Article describes why the use of cost-benefit analysis by the Office of Management and Budget to evaluate the change

²³ Daniel Wickler, *Persuasion and Coercion for Health: Ethical Issues in Government Efforts to Change Life-Styles*, 56 *Health & Society* 303–38 (1978), reprinted in Rolf Sartorius, *Paternalism* (Minnesota 1984).

suggested by this Article is inappropriate when dealing with novel ingredients in the context of individual risk.

II. NANOTECHNOLOGY USED IN CONSUMER PRODUCTS

The benefits of nanotechnologies are varied. On one hand, some claim that nanotechnology could provide the solution to global challenges such as providing a cure for cancer, a source for renewable energy, and the solution to the provision of clean water.²⁴ Others assert that nanotechnology could provide new medical treatments, reduced use of limited resources, and economic benefits.²⁵ On the other hand, nanoparticles used in consumer products offer far less important benefits. Nanotech cosmetics may improve appearance,²⁶ and nanotech sunscreens are transparent instead of white and pasty.²⁷ Some nanotech dietary supplement manufacturers claim that their products are better absorbed by the body.²⁸ Nanotechnology used in foods could provide more vivid colors and more potent flavors,

²⁴ Fabio Salamanca-Buentello, et al, *Nanotechnology and the Developing World*, 2 PLOS Med 0383, 0385 (2005). According to a study by the Canadian Program on Genomics and Global Health at the University of Toronto Joint Centre for Bioethics, the top ten applications of nanotechnology most likely to benefit developing countries, and which may contribute to the attainment of the United Nations Millennium Development Goals (MDGs), are as follows: energy storage; production and conversion; agricultural productivity enhancement; water treatment and remediation; disease diagnosis and screening; drug delivery systems; food processing and storage; air pollution and remediation; construction; health monitoring; vector and pest detection; and control. Id.

²⁵ The Royal Society and The Royal Academy of Engineering, *Nanoscience and Nanotechnologies: Opportunities and Uncertainties* *vii (July 2004), online at <http://www.nanotec.org.uk/report/Nano%20report%202004%20fn.pdf> (visited Sept 15, 2013).

²⁶ Cristina Buzea, Ivan I. Pacheco Blandino, and Kevin Robbie, *Nanomaterials and Nanoparticles: Sources and Toxicity*, 2 *Biointerphases* MR17, MR36 (2007) (discussing how engineered nanomaterials in cosmetic products regenerate skin cells, help maintain a youthful appearance of the skin, and hide wrinkles and creases).

²⁷ Natasha Singer, *New Products Bring Side Effect: Nanophobia*, NY Times E1 (Dec 3, 2008).

²⁸ William B. Schultz and Lisa Barclay, *A Hard Pill to Swallow: Barriers to Effective FDA Regulation of Nanotechnology-Based Dietary Supplements* *9 (Woodrow Wilson International Center for Scholars 2009), online at http://www.nanotechproject.org/process/assets/files/7056/pen17_final.pdf (visited Sept 15, 2013) (“Examples of product claims that tout special properties due to the use of nanotechnology include: increased effectiveness in a calcium/magnesium product; more rapid, uniform and complete absorption of nutrients in a spray form; increased absorption of a B12 vitamin spray; supplements that pass through membranes directly into human cells; and increased absorption of gel supplements by transforming fat-soluble nutrients into water-soluble ones.”).

nutritional additives, and antibacterial ingredients for food packaging.²⁹

To take advantage of some of these less socially beneficial improvements, engineered nanoparticles are pouring into everyday consumer products in steadily increasing amounts, resulting in a concomitant increase in consumer exposure to these novel ingredients. These nanoparticles are engineered to be only one to 100 nanometers in size.³⁰ To give an idea of just how small these nanoparticles are, a human hair is about 80,000 nanometers wide.³¹

Consumer products that use nanoscale materials can be found almost everywhere. Nanotech ingredients are in cosmetics, electronics, catalytics, magnetic and materials applications, as well as in drug delivery and medical imaging products.³² Just a small sampling of the specific products that contain nanotech ingredients includes cell phones, stain-

²⁹ *Toxic Nanoparticles Might Be Entering Human Food Supply*, ScienceDaily (Aug 22, 2013), online at http://www.sciencedaily.com/releases/2013/08/130822194530.htm?utm_source=feedburner&utm_medium=email&utm_campaign=Feed%3A+sciencedaily%2Ftop_news%2Ftop_health+%28ScienceDaily%3A+Top+News+---+Top+Health%29 (visited Sept 15, 2013).

³⁰ “Nanotechnology is the art and science of manipulating matter at the nanoscale to create new and unique materials and products.” Schultz and Barclay, *A Hard Pill to Swallow* at 20–23 (cited in note 28). The National Nanotechnology Initiative (“NNI”) is a federal research and development initiative that manages and coordinates the nanoscale research and technology endeavors of twenty-five different government agencies, including the FDA. The NNI considers nanotechnology to include activities that involve the following characteristics:

- (1) research and technology development at the atomic, molecular or macromolecular level, in the length scale of 1–100 nanometers; (2) creating and using structures, devices and systems that have novel properties and functions because of their small or intermediate size; and (3) ability to control or manipulate on the atomic scale.

Id.

³¹ The Royal Society and The Royal Academy of Engineering, *Nanoscience and Nanotechnologies* at viii–x (cited in note 25) (noting that a nanometer is one billionth of a meter.); National Nanotechnology Initiative, *What is Nanotechnology?* (nano.gov), online at <http://www.nano.gov/nanotech-101/what/definition> (visited Sept 15, 2013). To attempt to intellectualize just how small a nanoparticle is, compare nanoparticles to the thickness of a sheet of paper, which is roughly 100,000 nanometers wide, or to the size of a human hair, which is approximately 80,000 nanometers wide. National Nanotechnology Initiative, *Size of the Nanoscale* (nano.gov), online at <http://www.nano.gov/nanotech-101/what/nano-size> (visited Sept 15, 2013).

³² See, for example, Centers For Disease Control and Prevention, *Nanotechnology: Frequently Asked Questions*, online at <http://www.cdc.gov/niosh/topics/nanotech/faq.html> (visited Sept 15, 2013) (acknowledging the broad array of different categories of products that contain nanoparticles).

resistant clothing, sporting goods, digital cameras, eyeglasses, paints, and computers.³³

Importantly, some of these types of products use nanotech ingredients that are “fixed” inside a solid matrix: for example, cell phones, computers, and sporting goods, such as tennis racquets and golf clubs. This makes these types of nanotech ingredients less likely to move into the human body or the environment.³⁴ While nanotech ingredients that are manufactured and then “fixed” in consumer products are of less concern to consumers, they are of great concern to the workers who make the products as they are exposed to large amounts of these nanotech ingredients during the manufacturing process.³⁵

³³ See Hope Shand and Kathy Jo Wetter, *Shrinking Science: An Introduction to Nanotechnology*, in Linda Starke, ed., *State of the World 2006* 78, 80–82 (2006) (providing a list of various consumer products that containing nanotech ingredients); Project On Emerging Nanotech, *Nanotechnology Consumer Products Inventory*, online at <http://www.nanotechproject.org/inventories/consumer/browse/categories/> (visited Apr 3, 2013) (acknowledging the broad array of different categories of products that contain nanoparticles).

³⁴ The industry opines that fixed nanoparticles are unlikely to be absorbed by the human body or migrate into the environment. However, whether this is true is still being studied. See, for example, Singer, *New Products Bring Side Effect: Nanophobia*, NY Times at E1 (cited in note 27) (noting representatives of the cosmetic industry have stated that there was no evidence that nanotech personal care products are a health hazard). Dr. Andrew Maynard, the former chief science advisor to the Project on Emerging Nanotechnologies, states that: “I would be very surprised if [fixed carbon nanotubes are] dangerous to use, let us say, [in] a tennis racket or baseball bat[,] . . . [b]ut I do not think it is OK to tell people that we think it is safe—we’ve got to have evidence.” Ann Fernholm, *Carbon Nanotubes May Be as Harmful as Asbestos*, SF Chronicle C-1 (May 21, 2008). The unresolved problem is what happens when fixed nanoparticles are released as the result of natural wear and tear. For example, when a product breaks or the surface of one of these products is rubbed against the ground. Id. Dr. Maynard points out that the level of human exposure to asbestos as car brake pads containing asbestos wore down and roads paved with asbestos-containing materials deteriorated was high. See generally Agency for Toxic Substances and Disease Registry, United States Department of Health and Human Services, *Asbestos Toxicity*, online at <http://www.atsdr.cdc.gov/csem/asbestos/docs/asbestos.pdf> (visited Sept 15, 2013).

³⁵ See generally Department of Health and Human Services, *Current Intelligence Bulletin 65: Occupational Exposure to Carbon Nanotubes and Nanofibers* *1–2 (National Institute for Occupational Safety and Health Apr 2013), online at <http://www.cdc.gov/niosh/docs/2013-145/pdfs/2013-145.pdf> (visited Sept 15, 2013) (“NIOSH Bulletin”) (discussing the risks associated with exposure of workers to nanoparticles during the manufacturing process); Arthur Miller, et al, *Characterizing Exposures to Airborne Metals and Nanoparticle Emissions in a Refinery*, 54 *Annals of Occup Hygiene* 504, 511–12 (2010); R.J. Aitken, K.S. Creely, and C.L. Tran, *Nanoparticles: An Occupational Hygiene Review* 2–3 (Health and Safety Executive 2004), online at <http://www.hse.gov.uk/research/rrpdf/rr274.pdf> (visited Sept 15, 2013). Importantly, higher exposure levels may occur during cleaning and maintenance of production, research, and handling facilities. See NIOSH Bulletin at 1–2; Georgia Miller,

Products that contain predominantly “free” nanotech particles, such as liquid products, should be of more concern to consumers. Nanotech particles that are “free” are extremely mobile,³⁶ and the human body can absorb them through several different routes of exposure.³⁷ Nanoparticles can enter the blood stream through the skin,³⁸ the gastrointestinal tract,³⁹ or the lungs.⁴⁰ When inhaled, nanoparticles can invade all areas of the lungs.⁴¹ They can pass into the brain via the olfactory nerves⁴²

et al, *Nanomaterials, Sunscreens and Cosmetics: Small Ingredients, Big risks* *10 (Friends of the Earth Report 2006), online at http://libcloud.s3.amazonaws.com/93/ce/0/633/Nanomaterials_sunscreens_and_cosmetics.pdf (visited Sept 15, 2013). As the science on safe exposure levels and protective equipment in the work place is still changing, little is known about the levels at which workers can safely be exposed to nanoparticles while on the job. NIOSH Bulletin at 1–2. This is a pressing issue as it is estimated that, by 2015, over two million workers worldwide will be directly employed by industries using nanoparticles. Mihail C. Roco, *Converging Science and Technology at the Nanoscale: Opportunities for Education and Training*, 21 *Nature Biotech* 1247, 1248 (2003). It is likely that the numbers of workers employed indirectly in the supply chain will be significantly higher. Id (explaining that nanotechnology has the potential to create five million related jobs by 2015).

³⁶ David Rotman, *Measuring the Risks of Nanotechnology*, *Tech Rev* 71–73 (Apr 2003) (interviewing Dr. Vicki Colvin, Director of the Center for Biological and Environmental Nanotechnology at Rice University, about possibly unique health and environmental risks associated with nanotechnology); Buzea, Pacheco Blandino, and Robbie, 2 *Biointerphases* at MR44–48, MR50–57 (cited in note 26).

³⁷ Günter Oberdörster, et al, *Principles for Characterizing the Potential Human Health Effects from Exposure to Nanomaterials: Elements of a Screening Strategy*, 2 *Particle and Fibre Toxicology* 1, 2, 4 (2005).

³⁸ Cosmetics that use nanotech ingredients that are rubbed onto the skin contain nano-size particles 1000 nm in size. At this size, they can be absorbed through intact skin. Jillian Rouse and Jianzhong Yang, *Repetitive Motion Speeds Nanoparticle Uptake: ‘Bucky Amino Acid’ Penetrates Faster, Deeper When Skin Is Flexed*, *Sciencedaily* (Jan 9, 2007), online at <http://www.sciencedaily.com/releases/2007/01/070104144839.htm> (visited Sept 15, 2013) (noting that chemists and toxicologists find that uptake of nanoparticles through the skin is sped up through repetitive movement); Sally S. Tinkle, et al, *Skin as a Route of Exposure and Sensitization in Chronic Beryllium Disease*, 111 *Envir Health Persp* 1202, 1204–05 (2003) (presenting a study of the degree of penetration of nano-size particles into human skin). Damage to the skin can occur through sunburn, blemishes, shaving cuts, eczema, or other trauma. When skin is traumatized, nano-sized particles up to 7000 nm are absorbed by the skin. Günter Oberdörster, Eva Oberdörster, and Jan Oberdörster, *Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles*, 113 *Envir Health Persp* 823, 834 (2005). Importantly, many cosmetics and sunscreens containing nanotech ingredients are especially formulated to be used on damaged skin.

³⁹ Oberdörster, Oberdörster, and Oberdörster, 113 *Envir Health Perspectives* at 833–37 (cited in note 38); Peter H.M. Hoet, Irene Bruske-Hohlfeld, and Oleg V. Salata, *Nanoparticles: Known and Unknown Health Risks*, 2 *J Nanobiotech* 1, 1, 2–10 (Dec 2004).

⁴⁰ NIOSH Bulletin at 1–2 (cited in note 35).

⁴¹ Oberdörster, Oberdörster, and Oberdörster, 113 *Envir Health Persp* at 837 (cited in note 38); Hoet, Bruske-Hohlfeld, and Salata, 2 *J Nanobiotech* at 1–4 (cited in note 39).

and can also cross the formidable blood-brain barrier.⁴³ In contrast to macro-particles that are trapped and eradicated by the body's immune systems,⁴⁴ once nanoparticles are absorbed into the blood stream, they can travel unhindered into the muscles, liver, bone marrow, and spleen, and can actually move into cells.⁴⁵ Amazingly, nanoparticles can move through the cytoplasm and bind to cellular structures.⁴⁶ This includes the ability to get wedged in the mitochondria.⁴⁷ Finally, if absorbed by a pregnant woman, nanoparticles can cross the placenta, enter the fetus, and invade all of the areas listed above.⁴⁸

This use of free nanoparticles in food,⁴⁹ drugs,⁵⁰ cosmetics,⁵¹ dietary supplements,⁵² and sunscreens⁵³ creates a large and

⁴² Buzea, Pacheco Blandino, and Robbie, 2 *Biointerphases* at MR50–51 (cited in note 26); Alex Kirby, *Tiny Particles 'Threaten Brain'* (BBC News Jan 8, 2004), online at <http://news.bbc.co.uk/2/hi/science/nature/3379759.stm> (visited Sept 15, 2013); Annabelle Hett, *Nanotechnology: Small Matter, Many Unknowns* *17 (Swiss Reins Co 2004), online at http://media.swissre.com/documents/nanotechnology_small_matter_many_unknowns_en.pdf (visited Sept 15, 2013).

⁴³ Rotman, *Tech Rev* at 73 (cited in note 36); Buzea, Pacheco Blandino, and Robbie, 2 *Biointerphases* at MR51 (cited in note 26); Kirby, *Tiny Particles* at 17 (cited in note 42).

⁴⁴ Hett, *Nanotechnology* at 21 (cited in note 42).

⁴⁵ *Id.* at 22–23.

⁴⁶ Karen Florini, et al, *Nanotechnology: Getting It Right the First Time*, 3 *Nanotech L and Bus* 39, 42 (2006).

⁴⁷ Dusica Maysinger, et al, *Nanoparticles in Medicine*, in 3 *Oxford Handbook of Nanoscience and Technology: Applications* 503, 519 (A.V. Narlikar, et al, eds, 2010); Buzea, Pacheco Blandino, and Robbie, 2 *Biointerphases* at MR48 (cited in note 26).

⁴⁸ Karin S. Hougaard, et al, *Effects of Prenatal Exposure to Surface-Coated Nanosized Titanium Dioxide (UV-Titan): A Study in Mice*, 7 *Particle & Fibre Toxicology* 16, 22 (2010).

⁴⁹ See, for example, Georgia Miller and Rye Senjen, *Out of the Laboratory and on to our Plates: Nanotechnology in Food and Agriculture* *9 (Friends of the Earth 2008), online at http://www.foeurope.org/activities/nanotechnology/Documents/Nano_food_report.pdf (visited Sept 15, 2013) (stating nano-size additives can be found in some soft drinks, dairy products, sausages, beer, and other processed foods).

⁵⁰ See, for example, Christopher Weldon, Bozhi Tian, and Daniel S. Kohane, *Nanotechnology for Surgeons*, 3 *Wiley Interdisciplinary Rev: Nanomed & Nanobiotech* 223, 226 (2011) (discussing how the science of nanotechnology could create powerful new tools greatly enhancing surgeons' access to therapeutic and diagnostic measures); Kevin O'Donnell and Robert O. Williams, *Nanoparticulate Systems for Oral Drug Delivery to the Colon*, 8 *Intl J Nanotech* 4, 4–15 (2011) (arguing that by encapsulating a drug molecule within a nano-size module, a highly effective tool for controlling drug delivery to a specific target could be created, for example for the treatment of a cancerous tumor); Dorothy Farrell, et al, *Recent Advances from the National Cancer Institute Alliance for Nanotechnology in Cancer*, 4 *ACS Nano* 589 (2010) (noting nanotechnology holds great promise for the treatment of cancer).

⁵¹ See, for example, Miller and Senjen, *Out of the Laboratory* at 4 (cited in note 49).

⁵² See, for example, Schultz and Barclay, *A Hard Pill to Swallow* at 8 (cited in note 28). Dietary supplements with nanotech ingredients have jumped in number from eleven

growing level of consumer exposure to novel ingredients never before seen in nature. Nanotech ingredients are being used in rapidly increasing amounts to create “more potent food colourings, flavourings and nutritional additives, antibacterial ingredients for food packaging, and more potent agrochemicals and fertilisers.”⁵⁴ Food analysts estimate that nanotech food additives are being used in more than six hundred different food products.⁵⁵ Food packagers are also steadily increasing their use of nanotech particles in food packaging. This creates the opportunity for these particles to migrate into the food.⁵⁶

The National Institute of Occupational Safety and Health (“NIOSH”) reports that consumer products containing nanotech ingredients are being introduced into the market at a frequency of three to four per week.⁵⁷ Consumer products that contain nanotech ingredients number in the thousands,⁵⁸ while thousands of tons of nanoparticles are produced each year.⁵⁹ Nanotech research and development is predicted to reach \$3.1 trillion globally by 2015.⁶⁰ In 2007, \$147 billion in manufactured

in 2007 to forty-four in 2009. Id at 9.

⁵³ Id.

⁵⁴ Miller and Senjen, *Out of the Laboratory* at 4 (cited in note 49). Nanotech particle additives can be found in sodas, margarine, dairy products, and sausages. Id at 9. Another growing area is the use of nanotech content in food and beverage packaging, for example “nanoclay composites—plastics to which nanoscale clay platelets have been added.” Id at 4. These nanoclay materials are also used “in agriculture pipes and plastics to allow controlled release of herbicides.” Id.

⁵⁵ Stephen Daniells, *Think Big, Think Nano* (Foodnavigator.com Dec 19, 2007), online at <http://www.foodnavigator.com/Science-Nutrition/Think-big-think-nano> (visited Sept 15, 2013).

⁵⁶ Miller and Senjen, *Out of the Laboratory* at 4 (cited in note 49) (stating that between four hundred and five hundred foods have nanotech packaging).

⁵⁷ See, for example, Center For Disease Control and Prevention, *Nanotechnology: Frequently Asked Questions* (Sept 22, 2010), online at <http://www.cdc.gov/niosh/topics/nanotech/faq.html> (visited Sept 15, 2013) (acknowledging the broad array of different categories of products that contain nanoparticles).

⁵⁸ See Schultz and Barclay, *A Hard Pill to Swallow* at 20–23 (cited in note 28) (explaining that the increasing amounts of products integrating nanotechnology go unregulated, due to the dated FDA regulatory scheme).

⁵⁹ The Royal Society and The Royal Academy of Engineering, *Nanoscience and Nanotechnologies* at 26–27 (cited in note 25).

⁶⁰ Schultz and Barclay, *A Hard Pill to Swallow* at 8 (cited in note 28). See also *Buyer Beware: Product List Highlights Both Nanotech and Nano-marketing* (Electro IQ Mar 16, 2006), online at <http://www.electroiq.com/articles/stm/2006/03/buyer-beware-product-list-highlights-both-nanotech-and-nano-marketing.html> (visited Sept 15, 2013) (detailing the growing number of products containing nanoparticles); Center for Disease Control and Prevention, *Nanotechnology: Frequently Asked Questions* (cited in note 32).

goods using nanotech ingredients were produced.⁶¹ Unfortunately, the financial resources invested into the development, application, and production of nanoparticle technology is far more than the amount of money invested in the exploration of health and safety issues.⁶²

A. Why Are Nanotech Ingredients Novel?

Nanotech particles are unique. Nanoparticles and normal size particles have a whole range of fundamentally different properties. There are remarkable differences between the two in toxicity, bioaccumulation, persistence, chemical, magnetic, electrical, explosiveness, and optical characteristics.⁶³

Engineered nanoparticles differ significantly from their normal size counterparts⁶⁴ for two main reasons. First, the laws

⁶¹ Schultz and Barclay, *A Hard Pill to Swallow* at 8 (cited in note 28). See also *Buyer Beware: Product List Highlights Both Nanotech and Nano-marketing*, Electro IQ (Mar 16, 2006), <http://www.electroiQ.com/articles/stm/2006/03/buyer-beware-product-list-highlights-both-nanotech-and-nano-marketing.html> (detailing the growing number of products containing nanoparticles); Center for Disease Control and Prevention, *Nanotechnology: Frequently Asked Questions* (cited in note 32).

⁶² Compared to the amount of funding for nanotech commercial applications, the amount of money spent on health and environmental risks associated with nanotech products is very small. For example, as of 2010, only approximately 5 percent of the NNI's budget is dedicated to the health and environmental implications of this new technology. John F. Sargent Jr, *Nanotechnology and Environmental, Health, and Safety: Issues for Consideration* *11 (Congressional Research Service Jan 20, 2011), online at <http://www.fas.org/sgp/crs/misc/RL34614.pdf> (visited Sept 15, 2013).

⁶³ Buzea, Pacheco Blandino, and Robbie, 2 *Biointerphases* at MR17, MR23–25, MR47, MR59 (cited in note 26). See also Ernie Hood, *Nanotechnology: Looking as We Leap*, 112 *Envir Health Persp* A740, A741 (2004); The Royal Society and The Royal Academy of Engineering, *Nanoscience and Nanotechnologies: Opportunities and Uncertainties* at 5 (cited in note 25).

⁶⁴ In order to conform to the nomenclature adopted by the literature, this Article refers to particles that manifest these different properties as “nanoparticles” or “nanoscale” or “nano-sized” materials or versions and will refer to larger scale particles of the same chemical that do not have these unique properties as normal size materials or bulk materials. Buzea, Pacheco Blandino, and Robbie, 2 *Biointerphases* at MR23–25 (cited in note 26); The Royal Society and The Royal Academy of Engineering, *Nanoscience and Nanotechnologies: Opportunities and Uncertainties* at 7 (cited in note 25). For example, the list of FDA-approved active ingredients for use in sunscreens includes titanium dioxide for use up to a 25 percent concentration. Food and Drug Administration, *Sunscreen Drug Products for Over-The-Counter Human Use: Final Monograph*, 64 *Fed Reg* 27666, 27672 (May 21, 1999), to be codified at 21 *CFR* § 352 (“Final Monograph”). The safety and effectiveness of titanium dioxide in sunscreens was reviewed by the FDA prior to industry use of the engineered nanoparticle form of titanium dioxide pursuant to the normal process for over-the-counter (“OTC”) approval. Food and Drug Administration, *Small Business Assistance: Frequently Asked Questions on the Regulatory Process of Over-the-Counter (OTC) Drugs*, online at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm0>

of classical physics apply to normal size particles.⁶⁵ Comparatively, the laws of quantum mechanics apply to nanoparticles.⁶⁶ Second, nanoparticles enjoy an enormous surface-to-volume ratio, which translates into a greater proportion of atoms existing on the particle's surface.⁶⁷ As chemical reactions occur on the surface of particles, a nanoparticle has a greater potential for biological interaction. This means that nanoparticles are far more bioreactive than their normal size counterparts.⁶⁸ It is critical to note, as a public health matter, that this means that the inherent toxicity of any given quantity of nano-sized particles is much greater than the same quantity of their normal-sized counterparts.⁶⁹

69917.htm (visited Sept 15, 2013) (describing the process for OTC approval). The FDA stated that it is aware that sunscreen products use engineered nanoparticles but that it "does not consider micronized titanium dioxide to be a new ingredient but it considers it a specific grade of titanium dioxide originally reviewed by the Panel." 64 Fed Reg at 27671-72.

⁶⁵ Buzea, Pacheco Blandino, and Robbie, 2 Biointerphases at MR23 (cited in note 26) (stating the laws of classical physics don't apply to particles that are smaller than approximately 100 nanometers (nm)); The Royal Society and The Royal Academy of Engineering, *Nanoscience and Nanotechnologies: Opportunities and Uncertainties* at 7 (cited in note 25).

⁶⁶ Buzea, Pacheco Blandino, and Robbie, 2 Biointerphases at MR24-25 (cited in note 26) (noting the laws of quantum mechanics apply to nanoparticles affecting the magnetic, optical, and electric behavior of materials); The Royal Society and The Royal Academy of Engineering, *Nanoscience and Nanotechnologies: Opportunities and Uncertainties* at 7 (cited in note 25).

⁶⁷ Andre Nel, et al, *Toxic Potential of Materials at the Nanolevel*, 311 Sci 622, 622 (2006). Compared to macro-particles,

[T]his provides a greater surface area per unit mass. In the size range of < 100 nm, the number of surface molecules (expressed as a % of the molecules in the particle) is inversely related to particle size. For instance, in a particle of 30 nm size, about 10% of its molecules are expressed on the surface, whereas at 10 and 3 nm size the ratios increase to 20% and 50%, respectively. Because the number of atoms or molecules on the surface of the particle may determine the material reactivity, this is key to defining the chemical and biological properties of nanoparticles.

Id at 623 fig 1.

⁶⁸ Id at 622.

⁶⁹ Id; Scientific Committee on Emerging and Newly Identified Health Risks ("SCENIHR"), *Modified Opinion on the Appropriateness of Existing Methodologies to Assess the Potential Risks Associated with Engineered and Adventitious Products of Nanotechnologies* 13, 13 (European Commission 2005), online at http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003b.pdf (visited Sept 15, 2013).

B. What Are the Health Risks Associated with Exposure to Nanotech Ingredients?

Over the past several years, a number of scientific animal studies have started to provide at least some ideas about the type of negative health effects that can be expected to occur from exposure to the unique properties of nanotech ingredients. Some of the side effects could include a contribution to the development of neurodegenerative processes, such as Alzheimer's disease⁷⁰ or mesothelioma, the condition caused by asbestos.⁷¹

Studies show that there are two main negative physical effects that could cause these disorders.⁷² First, the increased bioreactivity of nanoparticles discussed above can harm living tissue.⁷³ Once inside cells, this enhanced bioreactivity can interfere with cell signaling, damaging the cell's structure and DNA.⁷⁴ In the opposite effect of the saying "the poison is in the dose," the smaller the size of the particle, the more likely it is to have a toxic effect because its bioreactivity increases.⁷⁵ For example, even if a material, like titanium dioxide, is harmless at a normal size, when it shrinks to nano-size, pulmonary toxicity increases.⁷⁶ Second, the human body contains scavenger cells

⁷⁰ Andre E. Nel, et al, *Understanding Biophysicochemical Interactions at the Nano-Bio Interface*, 8 *Nature Mat* 543, 550 (2009).

⁷¹ *Id* at 546.

⁷² See Jelena Kolosnjaj, Henri Szwarc, and Fathi Moussa, *Toxicity Studies of Carbon Nanotubes*, *Bio-Apps of Nanoparticles* 181 (Warren C.W. Chan ed 2007) (containing an exceptional survey of toxicity studies). For a comprehensive summary of the experimental mechanisms of nanotech toxicity, see Nel, et al, 8 *Nature Mat* at 551, table 4 (cited in note 70).

⁷³ Nel, et al, 8 *Nature Mat* at 543, table 4 (cited in note 70).

⁷⁴ Jirasak Wong-Ekkabut, et al, *Computer Simulation Study of Fullerene Translocation Through Lipid Membranes*, 3 *Nature Nanotech* 363, 363, 367 (2008); C.L. Tran, et al, *A Scoping Study to Identify Hazard Data Needs for Addressing the Risks Presented by Nanoparticles and Nanotubes*, *Institution of Occupational Medicine* 15, 25 (2005); Hisao Hidaka, et al, *In Vitro Photochemical Damage to DNA, RNA and Their Bases by an Inorganic Sunscreen Agent on Exposure to UVA and UVB Radiation*, 111 *J Photochem & Photobio* 205, 212 (1997); Rosemary Dunford, et al, *Chemical Oxidation and DNA Damage Catalysed by Inorganic Sunscreen Ingredients*, 418 *FEBS Letters* 87, 87-90 (1997).

⁷⁵ Qamar Rahman, et al, *Evidence That Ultrafine Titanium Dioxide Induces Micronuclei and Apoptosis in Syrian Hamster Embryo Fibroblasts*, 110 *Envir Health Persp* 797, 797, 799 (2002); T. Uchino, et al, *Quantitative Determination of OH Radical Generation and its Cytotoxicity Induced by TiO₂-UVA Treatment*, 16 *Toxicology in Vitro* 629, 634 (2002); Nel, et al, 311 *Sci* at 622 (cited in note 67).

⁷⁶ Tran, et al, *A Scoping Study*, at 21-23 (cited in note 74); Nel, et al, 311 *Sci* at 622

called phagocytes that eliminate foreign substances. These phagocytes can cease to function when they become clogged with nanotech particles.⁷⁷ This means that foreign particles, including bacteria, can invade the body with impunity as the phagocytes have been neutralized, causing an HIV-like effect.⁷⁸

While unfortunate, it is no surprise that there are very few animal studies of the health effects of exposure to nanoparticles in light of the relative amounts of investment in product development as compared to the investment in safety testing.⁷⁹ One of the first well-known animal studies observes the impact of exposures of nanoparticles called buckyballs⁸⁰ on fish.⁸¹ The result was that the brains of the fish, here largemouth bass, developed a toxic side effect that manifested itself in significant

(cited in note 67).

⁷⁷ Nel, et al, 8 *Nature Mat* at 550–52 (cited in note 70); Margot Lundborg, et al, *Human Alveolar Macrophage Phagocytic Function is Impaired by Aggregates of Ultrafine Carbon Particles*, 86 *Envir Rsrch Sect A86* 244, 252 (2001); Peter G. Barlow, et al, *Reduced Alveolar Macrophage Migration Induced by Acute Ambient Particle (PM10) Exposure*, 24 *Cell Bio & Toxicology* 243, 248–51 (2008); Buzea, Pacheco Blandino, and Robbie, 2 *Biointerphases* at MR45–46 (cited in note 26).

⁷⁸ Lundborg, et al, 86 *Envir Rsrch Sect* at 252 (cited in note 77); Barlow, et al, 24 *Cell Bio & Toxicology* at 251 (cited at 77); Buzea, Pacheco Blandino, and Robbie, 2 *Biointerphases* at MR45–46 (cited in note 26).

⁷⁹ See Sargent, *Nanotechnology and Environmental, Health, and Safety* (cited in note 62).

⁸⁰ Buckminsterfullerene (C60), called “buckyballs,” was named for Richard Buckminster Fuller, the famed engineer recognized for the creation of the geodesic dome. *Buckyballs Could Keep Water Systems Flowing*, *Sciencedaily* (Mar 12, 2009), online at <http://www.sciencedaily.com/releases/2009/03/090305080139.htm> (visited Sept 15, 2013).

⁸¹ Eva Oberdörster, *Manufactured Nanomaterials (Fullerenes, C60) Induce Oxidative Stress in the Brain of Juvenile Largemouth Bass*, 112 *Envir Health Persp* 1058, 1058 (2004). Buckyballs are soccer-ball-shaped, spherical molecules with sixty carbon molecules. They are the smallest of the fullerene family. T. Csörgő, M. Gyulassi, and D. Kharzeev, *Letter to the Editor, Buckyballs and Gluon Junction Networks on the Femtometre Scale*, 30 *J Physics G: Nuclear and Particle Physics* L17, L17–18 (2004); H.W. Kroto, et al, *Letters to Nature, C60 Buckminsterfullerene*, 318 *NATURE* 162, 162–63 (1985). Fullerenes are molecules made entirely of carbon. Csörgő, Gyulassi, and Kharzeev, 30 *J Physics G: Nuclear and Particle Physics* at L17.

lipid peroxidation.⁸² Buckyballs are commonly used in cosmetics,⁸³ food packaging, and dietary supplements.⁸⁴

Another startling set of recent, significant studies⁸⁵ suggests that another form of nanoparticle, called multi-walled carbon nanotubes,⁸⁶ could turn out to be as harmful as asbestos.⁸⁷ It

⁸² Oberdörster, 112 *Envir Health Persp* at 1060 (cited in note 81). See also Emil Venere, *'Buckyballs' Have a High Potential to Accumulate in Living Tissue*, *Purdue News* (Sept 18, 2008), online at <http://news.uns.purdue.edu/x/2008b/080918JafvertBuckyballs.html> (visited Sept 15, 2013) (interviewing author Chad T. Jafvert who explains that his research suggests that buckyballs have a greater probability of partitioning into fatty tissue than the banned pesticide DDT), referring to Chad T. Jafvert and Pradnya P. Kulkarni, *Buckminsterfullerene's (C60) Octanol—Water Partition Coefficient (Kow) and Aqueous Solubility*, 42 *Envir Sci & Tech* 5945, 5946–49 (2008).

⁸³ Bethany Halford, *Fullerene for the Face: Cosmetics Containing C60 Nanoparticles are Entering the Market even if Their Safety is Unclear*, 84 *Chem & Engineering News* 47, 47 (2006); Miller, et al, 54 *Annals of Occup Hygiene* at 7 (cited in note 35).

⁸⁴ Leslie Pray and Ann Yaktine, *Nanotechnology in Food Products: Workshop Summary*, *Inst of Med* 739, 741 (2009), online at http://www.nap.edu/catalog.php?record_id=12633 (visited Sept 15, 2013); Schultz and Barclay, *A Hard Pill to Swallow* at *9 (cited in note 28); Walter Derzko, *Novel, Safe Natural Food Supplement, Hydrated Fullerenes (C60-HyFn) or Water-Soluble Buckyballs Could Make 50–60% of the Riskier Synthetic Drugs and Pharmaceuticals Obsolete by 2025–30*, *Smart Economy* (May 17, 2010), online at http://smarteconomy.typepad.com/smart_economy/2010/05/novel-safe-natural-food-supplement-hydrated-fullerenes-c60hyfn-or-watersoluble-buckyballs-could-make.html (visited Sept 15, 2013); *Questioning Safety Of Nanotechnology in Your Vitamins*, *Sciencedaily* (Jan 15, 2009), online at <http://www.sciencedaily.com/releases/2009/01/090114114936.htm> (visited Sept 15, 2013); *Nanoparticles in Dietary Supplements Cause Health Concerns, Regulatory Challenges*, *Sciencedaily* (Feb 10, 2009), online at <http://www.sciencedaily.com/releases/2009/02/090209075633.htm> (visited Sept 15, 2013). The buckyballs negatively impacted the water habitat by killing all the water fleas and bacteria. Oberdörster, 112 *Envir Health Persp* at 1059 (cited in note 81). Another separate study showed that nanoparticles in small amounts are toxic to soil bacteria. J.D. Fortner, et al, *C60 in Water: Nanocrystal Formation and Microbial Response*, 39 *Envir Sci and Tech* 4307, 4307 (2005); *Buckyballs Could Keep Water Systems Flowing*, *Sciencedaily* (cited in note 80).

⁸⁵ Vincent Castranova, et al, *Persistent Pulmonary Fibrosis, Migration to the Pleura, and Other Preliminary New Findings After Subchronic Exposure to Multi-Walled Carbon Nanotubes*, *NIOSH Sci Blog* (Mar 19, 2009, 10:24 AM), online at <http://blogs.cdc.gov/niosh-science-blog/2009/03/nano-2/> (visited Sept 15, 2013) (“NIOSH Study”), reprinted as abstract in 108 *Toxicologist* 457 (2009); Craig A. Poland, et al, *Letters, Carbon Nanotubes Introduced into the Abdominal Cavity of Mice Show Asbestos-Like Pathogenicity in a Pilot Study*, 3 *Nature Nanotech* 423, 423–28 (2008); *Carbon Nanotubes that Look like Asbestos, Behave like Asbestos, Could Lead to Asbestos-Related Disease*, *Sciencedaily* (May 22, 2008), online at <http://www.sciencedaily.com/releases/2008/05/080520144004.htm> (visited Sept 15, 2013).

⁸⁶ “Discovered nearly 20 years ago, carbon nanotubes have been described as the wonder material of the 21st Century. Light as plastic and stronger than [sic] steel, they are being developed for use in new drugs, energy-efficient batteries and futuristic electronics.” *Carbon Nanotubes that Look Like Asbestos*, *Sciencedaily* (cited in note 85).

Carbon nanotubes are atom-thick sheets of graphite formed into cylinders. They may be formed from a single layer of graphite or they may consist of multiple concentric layers of graphite, resulting in multi-walled carbon

appears that these nanotubes have the potential to cause mesothelioma,⁸⁸ a cancer of the lung lining that appears following exposure to asbestos.⁸⁹ A pair of studies released in

nanotubes. While the diameter of a nanotube can vary from a few nanometers up to tens of nanometers, they can be hundreds or even thousands of nanometers long. Carbon nanotubes come in many forms, with different shapes, different atomic arrangements, and varying amounts and types of added chemicals—all of which affect their properties and might influence their impact on human health and the environment.

Id.

⁸⁷ Asbestos fibers are harmful because they are thin enough to penetrate deep into the lungs, but sufficiently long to confound the lungs' built-in clearance mechanisms for getting rid of particles. Widespread exposure to asbestos has been described as the worst occupational health disaster in U.S. history and the cost of asbestos-related disease is expected to exceed \$200 billion.

Id.

The toll of asbestos-related cancer, first noticed in the 1950s and 1960s, is likely to continue for several more decades even though usage reduced rapidly some 25 years ago. While there are reasons to suppose that nanotubes can be used safely, this will depend on appropriate steps being taken to prevent them from being inhaled in the places they are manufactured, used and ultimately disposed of. Such steps should be based on research into exposure and risk prevention, leading to regulation of their use.

Id (quoting Anthony Seaton, professor emeritus at the University of Aberdeen, UK). Similar to buckyballs, nanotubes are part of the fullerene family. They consist entirely of carbon molecules. Unlike buckyballs, nanotubes are made up of carbon atoms bonded into a tube shape, sometimes with a single wall, called single-wall carbon nanotubes ("SWCN"), or multiple walls, called multi-wall carbon nanotubes ("MWCN"). Marking on this similarity, carbon nanotubes are called "buckytubes" by some as their ends, when closed, take on the spherical shape of buckyballs. *Nanotubes and Buckyballs*, nanotechnologynow.com, online at <http://www.nanotech-now.com/nanotube-buckyball-sites.htm> (visited Sept 15, 2013).

⁸⁸ *Nanotubes and Buckyballs*, nanotechnologynow.com (cited in note 87).

⁸⁹ Id. In a 2008 study, nanoparticles were injected into the abdominal cavity of mice because this is a good predictor of how long fibers will affect the lung lining. Based on the study findings, it appears that long, thin, multi-walled carbon nanotubes that look like asbestos fibers, actually *behave* like asbestos fibers. This study suggests that people who breathe in nanotubes may develop cancer at some point after exposure. Poland, et al, 3 *Nature Nanotech* at 426–27 (cited in note 85). In 2009, only a year later, NIOSH took the Poland study one step further by examining the impact on mice of inhaling a small drop of liquid containing the multi-walled carbon nanotubes. See Castranova, et al, *Persistent Pulmonary Fibrosis* (cited in note 85). This study was the first to demonstrate that multi-walled carbon nanotubes aspirated by laboratory mice can actually migrate throughout even the tiniest area of the lungs and can actually migrate into the pleura. Id. See also LM Sargent, et al, *Induction of Aneuploidy by Single-Walled Carbon Nanotubes*, 50 *Envir Molecular Mutagenesis* 708, 713–15 (2009) (showing that single-walled carbon nanotubes can cause genotoxicity and abnormal chromosome number caused by interference with cell division (mitosis)); Atsuya Takagi, et al, *Induction of Mesothelioma in p53+/- Mouse by Intraperitoneal Application of Multi-Walled Carbon Nanotube*, 33 *J Toxicology Sci* 105, 110–14 (2008) (describing intraperitoneal injection of multi-walled carbon nanotubes causes mesothelial tumors in mice after). The mice had

May of 2013, completed by a consortium of seventy researchers from seven universities and the National Institute of Occupational Health and Safety, confirms that some types of nanoparticles are likely to cause physical harm.⁹⁰ This consortium was able to measure similar adverse health effects after exposure to nanoparticles by replicating their results in separate studies across multiple independent labs.⁹¹ In one study, laboratories measured pulmonary inflammation in rodents exposed to carbon nanotubes and nanotech titanium dioxide.⁹² In the second study, researchers demonstrated adverse reactions in cell cultures exposed to carbon nanotubes, nanotech titanium dioxide and nanotech zinc oxide.⁹³ Based on these collective studies, it appears that it is likely that carbon

persistent inflammation and fibrosis (scarring) in their lungs after inhaling the particles. Castranova, et al, *Persistent Pulmonary Fibrosis*, NIOSH Sci Blog (cited in note 85). These are important findings because multi-walled carbon nanotubes have properties that are similar to asbestos and a form of cancer called mesothelioma takes form in the pleura after exposure to asbestos. Id. The still unanswered question is whether MWCN will cause mesothelioma. Id. Answering this question, according to the authors of the study,

is of considerable importance, because research and business communities continue to invest heavily in carbon nanotubes for a wide range of products under the assumption that they are no more hazardous than graphite. Our results suggest the need for further research and great caution before introducing such products into the market if long-term harm is to be avoided.

Poland, et al, 3 *Nature Nanotech* at 423 (cited in note 85) (footnote omitted). Dr. Andrew Maynard, the co-author of the NIOSH study, opines that “[t]his study is exactly the kind of strategic, highly focused research needed to ensure the safe and responsible development of nanotechnology. . . . It looks at a specific nanoscale material expected to have widespread commercial applications and asks specific questions about a specific health hazard. Even though scientists have been raising concerns about the safety of long, thin carbon nanotubes for over a decade, none of the research needs in the current U.S. federal nanotechnology environment, health and safety risk research strategy address this question.” *Carbon Nanotubes that Look like Asbestos*, Sciencedaily (cited in note 85) (internal quotation marks omitted).

⁹⁰ See generally Robert Iafolla, *Groundbreaking Nanotechnology Studies Replicate Result Across Independent Labs*, 28 *BNA Toxics Law Reporter* 533 (May 9, 2013).

⁹¹ Id.

⁹² Id; *Interlaboratory Evaluation of Rodent Pulmonary Responses to Engineered Nanomaterials: The NIEHS NanoGo Consortium*, Environmental Health Perspectives, (May 6, 2013), online at <http://ehp.niehs.nih.gov/wp-content/uploads/121/5/ehp.1205693.pdf> (visited Sept 15, 2013).

⁹³ Iafolla, 28 *BNA Toxics Law Reporter* 533 (cited in note 90); *Intralaboratory Evaluation of In Vitro Cytotoxicity and Inflammatory Responses to Engineered Nanomaterials: The NIEHS NanoGo Consortium* (Environmental Health Perspectives May 6, 2013), online at <http://ehp.niehs.nih.gov/wp-content/uploads/121/5/ehp.1306561.pdf> (visited Sept 15, 2013).

nanotubes, nanotech titanium dioxide, and nanotech zinc oxide may pose a serious risk to human health.⁹⁴

C. FDA Regulation of Nanotech Consumer Products or FDA Regulations on Ingredient Labeling

Currently, the Food and Drug Administration (FDA) is regulating nanotech ingredients the same way that it regulates these ingredients' bulk counterparts.⁹⁵ If the macro-molecule version of an ingredient has previously been found by the FDA to be safe, for regulatory purposes, the FDA presumes that the

⁹⁴ See, for example, Kolosnjaj, *Toxicity Studies of Carbon Nanotubes*, Bio-Apps Of Nanoparticles at 181 (cited in 72) (opining that "available data clearly show that, under some conditions, nanotubes can cross the membrane barriers and suggests that if raw materials reach the organs they can induce harmful effects as inflammatory and fibrotic reactions"); Alexandra E. Porter, et al, *Direct Imaging of Single-Walled Carbon Nanotubes in Cells*, 2 Nature Nanotech 713, 713, 716 (2007) (showing that nanotubes can penetrate into cell "cytoplasm and localize within the cell nucleus, causing cell mortality in a dose-dependent manner"); Chiu-Wing Lam, et al, *A Review of Carbon Nanotube Toxicity and Assessment of Potential Occupational and Environmental Health Risks*, 36 Crit Rev in Toxicology 189, 207 (2006). See also A. Hubbs, et al, *Persistent Pulmonary Inflammation, Airway Mucous Metaplasia and Migration of Multi-Walled Carbon Nanotubes from the Lung After Subchronic Exposure*, 108 Toxicologist 457, 457 (2009) (describing how the fiber-like dimensions and durability of multi-walled carbon nanotubes, as well as their ability to cause inflammation in the abdominal cavity, are similar to asbestos); Elena Kisin, et al, *Pulmonary Response, Oxidative Stress and Genotoxicity Induced by Carbon Nanotubes*, 114 Toxicologist A793, A793 (2010) (finding acute inflammation and interstitial fibrosis in mice exposed to carbon nanofibers); Robert R. Mercer, et al, *Distribution and Persistence of Pleural Penetrations by Multi-Walled Carbon Nanotubes*, 7 Particle & Fibre Toxicology 1, 5–6 (2010) (demonstrating the toxic effects of MWCNTs because they can invade both the alveolar epithelium and visceral pleura); Jürgen Pauluhn, *Subchronic 13-Week Inhalation Exposure of Rats to Multi-Walled Carbon Nanotubes: Toxic Effects are Determined by Density of Agglomerate Structures, not Fibrillar Structures*, 113 Toxicology Sci 226, 226 (2010) (showing how rats exposed to carbon nanotubes at low doses have lower lung clearance); Dale W. Porter, et al, *Mouse Pulmonary Dose—and Time Course—Responses Induced by Exposure to Multi-Walled Carbon Nanotubes*, 269 Toxicology 136, 136–47 (2010) (observing the resemblance between asbestos fibers and the long and thin structures of common carbon nanotubes and carbon nanofibers and how both can migrate from pulmonary alveoli to pleural tissue, which is the same location where malignant mesothelioma develops).

⁹⁵ Katharine Van Tassel and Rose H. Goldman, *The Growing Consumer Exposure to Nanotechnology in Everyday Products: Regulating Innovative Technologies in Light of Lessons from the Past*, 44 U Conn 481, 503–13 (2010). Consistent with the nomenclature adopted by the literature, this Article will refer to particles that manifest these different properties as "nanoparticles" or "nanoscale" materials or versions and will refer to larger scale particles of the same chemical that do not have these unique properties as normal size materials or bulk materials. Buzea, Pacheco Blandino, and Robbie, 2 Biointerphases at MR23-25 (cited in note 26); The Royal Society and The Royal Academy of Engineering, *Nanoscience and Nanotechnologies: Opportunities and Uncertainties* at 7 (cited in note 25).

nanotech version is also safe.⁹⁶ Thus, the FDA is treating nanotech ingredients as bioequivalent to their normal size counterparts.⁹⁷

Regulating nanotech products exactly like their non-nanotech counterparts has serious consequences.⁹⁸ First, as manufacturers of food, dietary supplements, and cosmetics are not required to test their products for safety and are not required to obtain premarket approval from the FDA, the nanotech versions of these products are also not subject to these premarket steps.⁹⁹ With regard to sunscreens, nano-sized ingredients are deemed to be just as safe as their previously approved macro-sized ingredient counterparts, so no testing of these nano-ingredients is required.¹⁰⁰

Second, this regulatory stance of bioequivalence means that the listing of nanotech ingredients on product packaging is not required by the FDA. The FDA opines that product ingredient lists that refer to nanomaterial content by the same name as the normal size material counterpart are not false and misleading based on its presumption of bioequivalence. The FDA grounds this conclusion on its finding that *there is no scientific basis* on which to conclude that nanoscale materials *as a class* are inherently more *hazardous* than nonnanoscale materials.¹⁰¹ Thus, the FDA has taken the position that the fact that a consumer product contains nanotech ingredients is not “material” and need not be disclosed on labels.¹⁰²

⁹⁶ Van Tassel and Goldman, 44 U Conn at 503–15 (cited in note 95).

⁹⁷ Id.

⁹⁸ Id.

⁹⁹ Id.

¹⁰⁰ See note 64.

¹⁰¹ Food and Drug Administration, *Nanotechnology Task Force Report 2007*, online at <http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/UCM2006659.htm> (visited Sept 15, 2013).

¹⁰² Under the FDCA, a drug, device, food, dietary supplement, cosmetic, or sunscreen is deemed misbranded if its labeling is “false or misleading in any particular.” 21 USC § 362(a) (2006). See also 21 CFR § 701.1 (2011).

If an article is alleged to be misbranded because the labeling or advertising is misleading, then in determining whether the labeling or advertising is misleading . . . there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed

It is important to note that, while the FDA has recently acknowledged on its website that nanoparticles “can have chemical, physical, and biological properties that differ from those of their larger counterparts,”¹⁰³ the acknowledgment of the possibility that “nano can mean different” has yet to be given voice in any of the FDA’s regulatory positions on safety.

Third, conditioning the use of regulatory power to protect public health with the establishment of scientific evidence that will support a finding of *hazard*, will, as a general matter, be outcome determinative. This is because, as explained in the next section, the development of the scientific evidence needed to show a product is hazardous to health significantly lags behind the creation of the innovative technology itself. This regulatory posture means that there will be no regulatory protection of public health for perhaps decades.

Fourth, with regard to nanotech food, dietary supplements, sunscreens, and cosmetics, if the FDA does have concerns about their safety, it must use its seizure or injunctive powers to remove the product from the market.¹⁰⁴ In these court actions, the FDA has the burden of proving that the product is adulterated.¹⁰⁵ A product is adulterated if it “presents a

in the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.

21 USC § 321(n) (emphasis added). See also 21 USC § 331(a) (prohibiting the introduction into commerce of any food, device, or cosmetic that is misbranded); 21 USC § 343(a) (stating that foods are misbranded if their labeling is “false or misleading in any particular”); 21 USC § 352(a) (stating that drugs and devices are misbranded if their labeling is “false or misleading in any particular”); 21 USC § 362(a) (stating that cosmetics are misbranded if their labeling is “false or misleading in any particular”).

¹⁰³ Food and Drug Administration, *Nanotechnology*, online at <http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/default.htm> (visited Sept 15, 2013) (“The U.S. Food and Drug Administration (FDA) regulates a wide range of products, including foods, cosmetics, drugs, devices, veterinary products, and tobacco products, some of which may utilize nanotechnology or contain nanomaterials. Nanotechnology allows scientists to create, explore, and manipulate materials measured in nanometers (billionths of a meter). Such materials can have chemical, physical, and biological properties that differ from those of their larger counterparts.”).

¹⁰⁴ Richard A. Merrill, *Regulating Carcinogens in Food: A Legislator’s Guide to the Food Safety Provisions of the Federal Food, Drug, and Cosmetic Act*, 77 Mich L Rev 171, 186–90 (1978).

¹⁰⁵ 21 USC § 342(a)(I); Merrill, 77 Mich L Rev at 186–90 (cited in note 104). For a naturally occurring substance found in the food product, the food product is rendered adulterated if the substance is ordinarily injurious to health. 21 USC § 342(a)(I). However, if the substance in the food product is “added,” the food product is adulterated if the substance “may render” the food injurious to health. 21 USC § 342(a)(I).

significant or unreasonable risk of illness or injury.”¹⁰⁶ The FDA interprets “the plain meaning of ‘unreasonable’ . . . [to] connote [] comparison of the risks and benefit of the product.”¹⁰⁷ Thus, the FDA has the burden of “gathering data, soliciting comments and conducting the risk-benefit analysis.”¹⁰⁸

Once again, the FDA is likely to be unsuccessful using this route for a long period of time, perhaps decades, unless a great number of people have already been seriously injured. Even then, as the case of Ephedra demonstrates, it is likely to take a decade, or longer, for the FDA to be successful.¹⁰⁹

¹⁰⁶ 21 USC § 342(f)(1).

¹⁰⁷ Food and Drug Administration, Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk, 69 Fed Reg 6788, 6823 (Feb 11, 2004) (“Final Rule”).

¹⁰⁸ *Nutraceutical Corp v Andrew Von Eschenbach*, 459 F3d 1033, 1040 (10th Cir 2006) (“The plain meaning of ‘significant risk’ is a great danger.”).

¹⁰⁹ *Id.* at 1036. Ephedra was an ingredient that was commonly used in dietary supplements. *Id.* While ephedrine alkaloids occur naturally in some plants, ephedra falls into the same chemical category as the street drug called “speed.” Barry A. Palevitz, *Harmless Energizers or Dangerous Drugs?*, *The Scientist* (Dec 9, 2002), online at <http://www.the-scientist.com/?articles.view/articleNo/14399/title/Harmless-Energizers-or-Dangerous-Drugs/> (visited Sept 15, 2013) (“Ephedrine is a close relative of amphetamine, sometimes called benzedrene. A little chemical tinkering creates the street drugs methamphetamine and Ecstasy.”). Products containing ephedrine alkaloids were marketed as dietary supplements for weight loss and to enhance sports performance. See *Nutraceutical Corp*, 459 F3d at 1036. Over time, the FDA began receiving adverse event reports (“AERs”) from consumers, which included numerous complaints of heart attacks, strokes, seizures, and deaths associated with the consumption of products containing ephedrine alkaloids. See *id.* One of the most highly publicized cases of a fatal consequence from the use of ephedrine alkaloids in a dietary supplement was the death of Steve Belcher, a twenty-three-year-old baseball player with the Baltimore Orioles. See Fran Hawthorne, *Inside the FDA: The Business and Politics Behind the Drugs We Take and the Food We Eat* 57 (John Wiley and Sons 2005). In order to meet its burden of proof necessary to remove this ingredient from the market, the FDA took seven years to gather sufficient evidence on the safety of ephedrine alkaloids. The FDA compiled an administrative record of 130,000 pages, 19,000 AERs, and engaged in extensive notice and comment before it passed a regulation banning the sale of products containing ephedrine alkaloids in 2004. See 69 Fed Reg at 6788 (cited in note 107); *Nutraceutical Corp*, 459 F3d at 1036. In this final rule, the FDA stated that “[t]he best clinical evidence for a benefit . . . supports only a modest short-term weight loss, insufficient to positively affect cardiovascular risk factors or health conditions associated with being overweight or obese.” *Nutraceutical Corp*, 459 F3d at 1036–37. Then, the FDA had to spend several additional years in litigation until Ephedra was finally taken off the market. The manufacturer of Ephedra filed suit, arguing that the FDA had failed to meet its burden of proof of showing that products containing ephedrine alkaloids were unsafe. *Id.* at 1043–44. The district court found for the manufacturer; however, in 2006, the FDA prevailed on appeal. *Id.* at 1038–39. The total time and expense involved in this process, including the cost of the harm suffered by consumers, was tremendous. 69 Fed Reg at 6788 (cited in note 107). Not only did this proceeding take almost a decade, the amount of time and money that was spent by the FDA, which it could have used on other matters, was enormous. It is worth pointing out that the taxpayers foot the bill for this

D. Impact of the FDA's Focus on Hazard to Trigger Public Health Safety Regulation

The FDA's reliance on hazard to trigger the use of its regulatory power to protect public health when innovative ingredients are used in consumer products short-circuits its ability to act for sometimes-lengthy periods of time. This is because a substantial lag time, likely a decade or more, invariably exists between the production and distribution of the innovative technology to the public and the development of the science necessary to identify the risks associated with that technology. This lag time occurs when a manufacturer is not required by the FDCA to prove safety before being allowed to market a novel, innovative product as there is, otherwise, little incentive to invest in the testing process to prove safety. The cost of testing for safety is, instead, born by third parties—almost entirely the government and, thus, the taxpayers¹¹⁰—and is performed after the product has already been introduced into

effort, not the manufacturers who reaped tremendous profits over several decades from marketing Ephedra.

¹¹⁰ Ian Urbina, *Think Those Chemicals Have Been Tested?*, NY Times (April 13, 2013), online at <http://www.nytimes.com/2013/04/14/sunday-review/think-those-chemicals-have-been-tested.html> (visited Sept 15, 2013). “Many Americans assume that the chemicals in their shampoos, detergents and other consumer products have been thoroughly tested and proved to be safe. This assumption is wrong. Unlike pharmaceuticals or pesticides, industrial chemicals do not have to be tested before they are put on the market.” *Id.*

Companies have to alert the Environmental Protection Agency before manufacturing or importing new chemicals. But then it is the E.P.A.'s job to review academic or industry data, or use computer modeling, to determine whether a new chemical poses risks. Companies are not required to provide any safety data when they notify the agency about a new chemical, and they rarely do it voluntarily, although the E.P.A. can later request data if it can show there is a potential risk. If the E.P.A. does not take steps to block the new chemical within 90 days or suspend review until a company provides any requested data, the chemical is by default given a green light. The law puts federal authorities in a bind. ‘It’s the worst kind of Catch-22,’ said Dr. Richard Denison, senior scientist at the Environmental Defense Fund. ‘Under this law, the E.P.A. can’t even require testing to determine whether a risk exists without first showing a risk is likely.’ As a result, the overwhelming majority of chemicals in use today have never been independently tested for safety. In its history, the E.P.A. has mandated safety testing for only a small percentage of the 85,000 industrial chemicals available for use today. And once chemicals are in use, the burden on the E.P.A. is so high that it has succeeded in banning or restricting only five substances, and often only in specific applications: polychlorinated biphenyls, dioxin, hexavalent chromium, asbestos and chlorofluorocarbons.

Id.

the market. Thus, the focus on hazard means that the FDA must wait to regulate to protect public health until the state of the science on health risks catches up to the innovation itself. During this scientific lag time, manufacturers are free to market their products with no interference and no notice to unsuspecting consumers.¹¹¹ As explained in the next section, this Article refers to this scientific lag time as the health risk information void.

1. The health risk information void.

When a manufacturer is not required to prove safety before being allowed to market a novel, innovative product, it is common for the development of novel technologies to far outpace the development of the science necessary to test for the health risks associated with these technologies.¹¹² This scientific lag time creates a period during which there is an information void with regard to risks to human health. As this information void is slowly filled through scientific experimentation, the level of uncertainty over health risks commonly progresses from *ignorance* (where scientists don't know what they don't know) to *indeterminacy* (where scientists know what they don't know, but can plan the scientific experiments necessary to find out) to, finally, a tipping point in the state of knowledge when *classic probability analysis* can be applied to predict, or quantify, risk levels to human health.¹¹³ Thus, as health risks take time to quantify, the result of the reliance on establishing hazard through the use of risk/benefit analysis as a precondition to regulation to protect public health is a foregone conclusion when many new technologies first enter the market. The practical result is that an unsafe product containing an innovative, novel

¹¹¹ John M. Broder, *New Alliance Emerges to Tighten Chemical Rules*, NY Times (May 24, 2013), online at <http://www.nytimes.com/2013/05/25/us/politics/lautenbergs-chemical-safety-bill-gains-momentum.html?pagewanted=all> (visited Sept 15, 2013) (“Of roughly 85,000 chemicals registered for use in the United States, only 200 have been tested by the Environmental Protection Agency and fewer than a dozen—including polychlorinated biphenyls, dioxin and hexavalent chromium—have been restricted.”).

¹¹² Nicholas A. Ashford, *The Legacy of the Precautionary Principle in U.S. Law: The Rise of Cost-Benefit Analysis and Risk Assessment as Undermining Factors in Health, Safety and Environmental Protection*, in Nicolas de Sadeleer, ed., *Implementing The Precautionary Principle: Approaches From The Nordic Countries, The EU and The United States* 356–61 (Routledge 2006).

¹¹³ *Id.*

ingredient is likely to remain on the market for a long period of time before the FDA can take action.

a) *Examples of lag times with serious health consequences.* There are numerous examples¹¹⁴ of the negative impact on public health of this lag time between the introduction of new chemical compounds and innovative technologies into the market and the development of the science necessary to identify the associated hazard to human health.¹¹⁵ For example, it took decades to develop the science necessary to establish the endocrine disruption hazard caused by novel product ingredients such as polychlorinated biphenyls (“PCBs”), tributyltin (“TBT”), diethylstilbestrol (“DES”), Thalidomide, and the Great Lakes pollution.¹¹⁶ Illustratively, some evidence existed in the 1930s that PCBs were a serious hazard to human health.¹¹⁷ However, it took four decades before the state of the science evolved to the point of identifying the extent of the hazard to human health. Sweden was the first country to ban PCBs in the 1970s, with the European Union following suit in 1996.¹¹⁸

Other examples include those of medical x-rays, benzene, and asbestos. The first scientific warnings over medical x-rays occurred in 1896, those relating to benzene occurred in 1897, and those relating to asbestos occurred in 1898. Yet it took between thirty (for PCBs)¹¹⁹ and one hundred years (for x-

¹¹⁴ For a comprehensive analysis of fourteen case studies of these types of scenarios, see European Environmental Agency, *Late Lessons From Early Warnings: The Precautionary Principle 1896–2000*, 22 *Envir Issue Rpt*, 66–69 (2001).

¹¹⁵ Urbina, *Think Those Chemicals Have Been Tested?*, *NY Times* (cited in note 110).

¹¹⁶ David Gee, *Late Lessons from Early Warnings: Toward Realism and Precaution with Endocrine-Disrupting Substances*, 114 *Envir Health Persp* 152, 156 (2006). See also Katharine A. Van Tassel, *Slaying the Hydra: The History of Quack Medicine, the Obesity Epidemic and the FDA’s Battle to Regulate Dietary Supplements Marketed as Weight Loss Aids*, 6 *Ind Health L Rev* 203, 228–29 (2009) (discussing the case of Thalidomide).

¹¹⁷ European Environmental Agency, 22 *Envir Issue Rpt* at 66–69 (cited in note 114).

¹¹⁸ *Id.* at 126. In 1962, the book *Silent Spring* warned of the negative health effects on humans and wildlife of this exposure. The marketing of these novel chemicals continued unabated in spite of this warning. And the full extent of the devastating consequences to the Great Lakes area of a five decades-long period of human and environmental exposure to pesticides with the novel organochlorine compound ingredients is still unknown. See generally Rachel Carson, *Silent Spring* (Houghton Mifflin Harcourt 1962).

¹¹⁹ Gee, 114 *Envir Health Persp* at 155 (cited in note 116). Another example is the introduction of CFCs. CFCs have created the ozone hole, resulting in thousands of additional skin cancer cases that will only peak in number in the middle of this century. *Id.* at 155–56.

rays)¹²⁰ for scientists to determine the extent of these hazards and then for regulations to be promulgated to mitigate the already extensive damage to public health caused by these products.

b) *Nanotech ingredients and the health risk information void.* While the use of nanoparticles in consumer products and the resultant exposure of consumers are growing daily, the body of science necessary to identify the health risks associated with engineered nanoparticles is still in its infancy. When the FDA first made its decisions on how to regulate nanotech products, far less was known about the distinctive properties of nanoparticles, their uniquely high level of bioreactivity, and the resultant heightened potential for adverse health effects. Scientists simply “did not know what they did not know” about the health risks associated with nanotech particles. At that point in time, the FDA made its regulatory choices in an environment of ignorance, choosing to regulate based on what scientists now know to be a false assumption of bioequivalence.

Over the past several years, a parade of major scientific discoveries has shifted the nature of the uncertainty over the public health risks of nanotech particles from ignorance to indeterminacy.¹²¹ In other words, scientists have progressed from *not knowing* what they do not know, to *knowing* what they do not know. Scientists now understand that engineered nanoparticles may create novel health risks caused by powerful nano-bio interactions that have never before existed in nature.

In order to move from indeterminacy to classic risk analysis, scientists must still determine the nature and extent of the harm that occurs as a result of these nano-bio interactions. Then, using classic risk analysis, scientists must quantify the probability and degree of those harms. Thus, the new awareness on the part of scientists that nanoparticles can cause serious physical harm, and the identification of some of the potential mechanisms for causation, opens the door to the ability to plan out the systematic study of each new type of engineered nanoparticle in order to eliminate or confirm the associated health risks. In spite of the fact that the state of the science has now moved into indeterminacy, the FDA’s reliance on establishing hazard through the use of classic risk/benefit

¹²⁰ European Environmental Agency, 22 *Envir Issue Rpt* at 66–69 (cited in note 114).

¹²¹ See Part II.B.

analysis in making decisions over whether to regulate for safety means that, until the science on the health risks associated with nanoparticles has matured to the point that the risks can be quantified, the FDA will proceed as if this growing body of science did not exist.

As explained in the next section, switching the FDA's regulatory focus onto novelty, rather than hazard, enables the public health product safety net, which can act to safeguard the public while this ponderous cycle of scientific inquiry runs its course.

2. The FDA's focus on hazard disables the public health product safety net.

The public health safety net is a powerful, interactive network that involves consumers as well as the healthcare system, the state and federal public health protection agencies, and the tort system. Importantly, ingredient listing is essential to the creation of this safety net—without this listing, the safety net unravels into nothing. To summarize, novel ingredient listing protects consumer safety through consumer self-protection. If a consumer knows that she is being exposed to a novel ingredient, she can use heightened vigilance to watch for symptoms of harm. It also allows for the appropriate treatment of injured consumers by medical professionals who can identify novel ingredients as potential causative agents through accurate exposure reporting by consumers. Ingredient listing is also necessary to the proper reporting of injury-causing agents to state and federal public health protection agencies that manage the early warning and product recall systems. Finally, the data collected by these public health protection agencies makes up the evidence required to enable the instrumental use of the tort system, which encourages the proper investment by manufactures in product safety and protects against the overuse and overconsumption of harmful products by consumers. Together, these public and private actors join to form the public health product safety net.

a) Negative impact on consumer self-protection, medical treatment, and the early warning and product recall systems. The FDA's current focus on hazard means that it can't act to regulate nanotech ingredients until each separate variety of nanoparticle is proved to be hazardous to human health. Recall

that the number of different varieties of nanoparticles is only limited by the creativity and ingenuity of engineers and scientists so that this may number in the tens of thousands. Until each variety of nanoparticle is proven to be hazardous to human health, nanotech products will continue to be regulated like their macro-sized counterparts. This means that nanoparticles will not be listed on ingredient labels. Thus, the FDA's focus on hazard to trigger its authority to require ingredient listing means that consumers are unaware of the extent of their exposure to novel nanotech substances. This lack of knowledge bars the ability of public health officials to monitor whether the heavy exposure of US consumers to nanotech products is causing acute or latent toxic reactions. Consequently, it is currently highly unlikely that any potential health risks to the population from this exposure can be identified and eliminated.

For example, if a consumer uses a nanotech product and has a toxic reaction, the consumer will assume that the reaction is to the product itself, not an exposure to the nanoparticle ingredient because the new nanotech ingredient is not listed on the product label. The only result is that the consumer will avoid that particular product in the future. A mild reaction will not merit a visit to a physician and will go unreported.

If the reaction is moderate to severe, a physician may be consulted. If the physician reports the adverse reaction, it will be incorrectly reported as a reaction to the particular host product based on the inaccurate information given by the patient. It will not be correctly reported as a reaction to the host product's nanotech ingredients.

This misinformation has a broader impact in light of the new way scientists are using big data collected through social media to proactively identify product safety problems. "Using data drawn from queries entered into Google, Microsoft, and Yahoo search engines, scientists at Microsoft, Stanford, and Columbia University have for the first time been able to detect evidence of unreported prescription drug side effects before they were found by the Food and Drug Administration's warning system."¹²² Another group of scientists are using data analysis

¹²² John Markoff, *Unreported Side Effects of Drugs are Found Using Internet Search Data, Study Finds*, NY Times (March 6, 2013), online at <http://www.nytimes.com/2013/03/07/science/unreported-side-effects-of-drugs-found-using-internet-data-study->

tools to analyze social media, including tweets and on-line discussion forums, to identify adverse drug reactions.¹²³ These scientists

retroactively analyzed four types of public on-line media (websites, blogs, Web forums and social networking sites) posted from 2000 to early 2012 and were able to identify hundreds and thousands of documents containing adverse drug reaction-related information. The preliminary results suggest that these documents can accurately provide warnings earlier—in some cases years earlier—than existing channels.¹²⁴

In the context of food safety, several apps have been developed to help public health officials track food-borne illnesses using data collected from Twitter.¹²⁵ These big data strategies are just the start of muscular new additions to product safety surveillance systems representing a fundamental shift from a reactive to proactive monitoring systems. However, if consumers are not provided accurate information on the innovative new ingredients in consumer products, this revolutionary data collection system can't be used by scientists or public health officials to monitor the safety of novel, innovative ingredients, such as those using nanotechnology.

The bottom line is that the FDA's decision that manufacturers need not list nanotech ingredients on package labels means that the public health system in place for collecting data on the harms from exposures to novel ingredients had been disabled. This means that the key elements of the public health product safety net have been deactivated: (1) a consumer cannot engage in self-protection and avoid the novel ingredient if it is causing injury; (2) a consumer's ability to obtain appropriate medical treatment if injured has been sabotaged as they can't correctly inform their physicians what new ingredients they have been exposed to; (3) physicians and consumers can't

finds.html?_r=0 (visited Sept 15, 2013).

¹²³ H. Brey Cannon, *Research to Sift Social Media for Early Signs of Adverse Drug Reactions*, UVA Today (Sept 20, 2012), online at <http://news.virginia.edu/content/research-sift-social-media-early-signs-adverse-drug-reactions> (visited Sept 15, 2013).

¹²⁴ Id.

¹²⁵ Krietsch, *Social Media Apps* (cited in note 20); *Tracking Twitter May Enhance Monitoring of Food Safety at Restaurants*, ScienceDaily (cited in note 20).

contribute to, or benefit from, the early warning system that gives notice to consumers that a product is causing injuries to some people so as to trigger heightened vigilance by all; and (4) the product recall systems that all consumers rely upon to protect against personal injury from unsafe products does not work for novel ingredients.

b) *Negative impact on the tort system.* While the prime objective of the tort system is to compensate innocent victims harmed by defective products, shifting the cost of these injuries onto the manufacturers is also instrumental to the proper functioning of the public health product safety net. Forcing a manufacturer to bear the costs of injuries incurred from its products that are faulty in their manufacture or design may deter future misconduct and may tacitly encourage more careful behavior, such as increasingly diligent testing and product design.

The cost of injuries from the use of a product may also then be built into the price of the product and passed on to the consumer. If these effects are realized, several additional goals of the public health product safety net are furthered. First, the cost of the risk will be borne by all of those using the product generally through the increased price, instead of the innocent victim alone. Second, the price of the product will reflect its true social cost. This price will then mediate consumer choice, more likely resulting in optimum levels of production and purchase. As the price of the product increases as a result of manufacturers' internalizing the cost of injuries to product users, the consumption of the product will likely decline as consumers switch to less costly alternatives, resulting, ultimately, in a decrease in injuries due to the fall in the use of the product. Thus, the tort system is an important part of the public health product safety net as it insulates against the overuse and overconsumption of relatively risky products.

Moreover, as a part of the public health product safety net, the tort system places the cost of injury avoidance on the least-cost accident avoider. The manufacturer is often in the best position to accurately access the various ways of avoiding costs of injuries through redesign, quality control, and other safety measures. As a result of its level of access, the manufacturer is also often in the best position to insure against future injuries. Internalizing all of these costs—as well as the costs associated with injuries—into the price of the product may ultimately force

a manufacturer to consider the true cost of certain products when making its choices of which products to produce. It is hoped that the end result of this part of the public health product safety net is a socially-efficient output.

However, this cascade of beneficial effects that can occur from the proper use of the tort system is short-circuited when the FDA focuses on hazard to regulate innovative products. The principle reasons for this result are three-fold. First, as nanotech ingredients are not required to be listed on product labels, the consumer will not know that she was exposed to a nanotech ingredient. Thus, the consumer is unlikely to suspect that her injuries were caused by a novel substance.¹²⁶ Second, if the consumer learns that a nanotech ingredient was the cause of her injury, she will be required to establish proximate cause under tort law by showing that the manufacturer could have foreseen the risk of harm.¹²⁷ As with many new technologies, the rate of the introduction of nanotech products into the market has far outpaced the science needed to demonstrate its associated risks. Under either the *Daubert*¹²⁸ or *Frye*¹²⁹ tests, this research lag acts to insulate a manufacturer from liability based on a lack of causation¹³⁰ and foreseeability.¹³¹

The final hurdle arises in the context of both negligence and strict liability claims. The lack of labeling means that the public health protection agencies, such as the Center for Disease Control (CDC) and the FDA, cannot collect the data that, over time, could accumulate to the point of meeting the evidentiary hurdles of causation and foreseeability. Over and above this problem, unless the consumer can establish that she is a

¹²⁶ Katharine Van Tassel, *The Introduction of Biotech Foods to the Tort System: Creating a New Duty to Identify*, 72 U Cin L Rev 1645, 1681 (2004).

¹²⁷ *Id* at 1683–84.

¹²⁸ See *Daubert v Merrell Dow Pharmaceuticals, Inc*, 509 US 579, 589 (1993).

¹²⁹ See *Frye v United States*, 293 F 1013, 1014 (DC Cir 1923).

¹³⁰ Under the *Daubert* and *Frye* standards, evidentiary principles are likely to bar any introduction of scientific evidence to meet the burden of proof on causation as long as there is scientific uncertainty. *Daubert*, 509 US at 589; *Frye*, 293 F at 1014. The *Daubert* factors counsel judges to ask the following questions in making decisions on the admissibility of scientific evidence: (1) Has the technique been tested in actual field conditions (and not just in a laboratory)?; (2) Has the technique been subject to peer review and publication?; (3) What is the known or potential rate of error? Is it zero, or low enough to be close to zero?; (4) Do standards exist for the control of the technique's operation?; and, (5) Has the technique been generally accepted within the relevant scientific community? *Daubert*, 509 US at 580.

¹³¹ Van Tassel, 72 U Cin L Rev at 1683–84 (cited in note 126).

member of a substantial class of people who are at risk for the same type of adverse reaction, the case is likely to be dismissed under what is commonly referred to as the “idiosyncratic plaintiff defense.”¹³² This “*de minimus* harm” liability threshold can range from tens of thousands to millions of people.¹³³ As with causation, because nanotech ingredients in consumer products are unlabeled, injured consumers are unlikely to recognize what actually caused their injuries. As a result, these injuries will go unreported. Without this data, a consumer will be unable to establish that she is a member of a substantial class, creating an almost impassable barrier to recovery.¹³⁴

The bottom line is that the FDA’s no-labeling decision means that another key element of the public health product safety net, the tort system, has also been disabled.

III. HISTORY OF FDCA REGULATION OF NOVEL INGREDIENTS

As explained in the prior section, the current focus by the FDA on hazard to trigger regulation of novel, innovative ingredients in the context of scientific uncertainty fosters innovation but does nothing to protect public health. In the past, the FDA has avoided this problem by focusing on novelty rather than on hazard. As described in the next sections, this focus had a domino effect that created the public health product safety net that managed the scientific uncertainty over possible negative health effects of these novel ingredients. This focus on novelty also fits with the overall scheme of the FDCA, which titers the degree and kind of regulation it uses to protect consumers from harm from third parties to the level and type of vulnerability of a product’s targeted consumers. The overall result was that an appropriate balance between public health protection and innovation was achieved. A look back at this history explains why, and how, this balance was realized in the past and how it can be reached in the modern day context of rapidly emerging innovative technologies.

¹³² Id at 1680, 1683–84. This defense is basically a contention that a reasonable consumer would not have had the reaction and that the defect is in the consumer, not the product. Id.

¹³³ Id.

¹³⁴ Id.

A. The Pure Food Act of 1906

In the 1850s, a large majority of Americans lived and worked on farms.¹³⁵ Grain was milled at the local level by thousands of mills and rural areas were peppered with hundreds of small packing plants that packaged all of the locally produced foods.¹³⁶ By the turn of the century, the majority of the population moved to the city, a far smaller number of mills did the vast majority of the work, and packaging companies grew in size, dwindled sharply in number, and moved to the cities.¹³⁷ Food produced locally was shipped to these big city packing companies, packaged in cans and jars and was then returned, “watered down, preserved and cheap.”¹³⁸ Soon, these products were moving across great distances as horses were replaced with cars, trucks, and trains. Food, clothing, and simple tools were no longer made by people for their own use and the use of their neighbors. “The modern estrangement between the people who create goods and the people who consume them now emerged.”¹³⁹ This “modern estrangement”

made adulteration and deception both easy and profitable as manufacturers of food and medicines no longer had to face their customers. Under laissez-faire regulation, corruption and abuse were rampant. Food producers scammed consumers by adding fillers to food to increase weight (such as chalk, clay, or plaster of paris to flour and ground up insect carcasses, commonly lice, to brown sugar). Large amounts of untested chemicals (such as formaldehyde, sulfites, borax, salicylic acid and benzoic acid) were used liberally to preserve food for transport and to disguise the taste and appearance of food that was spoiled.¹⁴⁰

¹³⁵ Phillip J. Hilts, *Protecting America's Health: the FDA, Business, and One Hundred Years of Regulation* 11 (UNC 2004).

¹³⁶ Id.

¹³⁷ Id at 12.

¹³⁸ Id.

¹³⁹ Hilts, *Protecting America's Health* at 12 (cited in note 135).

¹⁴⁰ Van Tassel, 6 Ind Health L Rev at 230 (cited in note 116). See also Hilts, *Protecting America's Health* at 21–22 (cited in note 135) (“Copper sulfate can make faded vegetables appear green again; sodium benzoate can prevent decayed tomatoes from rotting altogether; stearins can stretch lard; borax can make odorous ham acceptable

Milk became one of the most adulterated products at the turn of the century. It was frequently watered down or mixed with formaldehyde, causing the deaths of numerous children.¹⁴¹

This was the state of affairs until Upton Sinclair's book *The Jungle* was published in 1905.¹⁴² *The Jungle* exposed the filthy and appalling conditions for workers in meat packing factories.¹⁴³ An unintended consequence was to turn the stomachs of the nation who read about men with tuberculosis who spit globs of bloody mucous onto filthy, factory floors. The workers then dragged dead, skinned carcasses along these same filthy, contaminated floors to the cutting tables.¹⁴⁴ In an attempt to deal with these problems, Congress first passed the Pure Food and Drug Act of 1906 ("1906 Act"), creating the first federal law prohibiting the interstate transportation and sale of adulterated food or drugs.¹⁴⁵

B. The Food Drug and Cosmetic Act of 1938

Unfortunately, the 1906 Pure Food Act did not anticipate two subsequent major developments: the processed food revolution and a series of Supreme Court cases that eviscerated the 1906 Act leaving unchecked the remarkable growth of quack medicines.¹⁴⁶

New food processing techniques triggered the processed food revolution that swept across the country between the 1930s and 1950s. This new processed and packaged food created a black box for consumers. For example, jelly had customarily been half sugar and half fruit.¹⁴⁷ But Strawberry BRED-SPRED did not

when canned."); Food and Drug Administration, *The Long Struggle for the 1906 Law* (June 1981), online at <http://www.fda.gov/AboutFDA/WhatWeDo/History/CentennialofFDA/TheLongStrugglefortheLaw/> (visited Sept 15, 2013).

¹⁴¹ Richard M. Cooper, *The Struggle for the 1906 Act*, in *FDA: a Century of Consumer Protection* 28 (Wayne L. Pines, ed, 2006) ("Milk was one of the most adulterated products in America at the turn of the century; it was frequently watered down and preserved with formaldehyde.").

¹⁴² Id.

¹⁴³ Id.

¹⁴⁴ Id.

¹⁴⁵ Pure Food and Drug Act of 1906, Pub L No 59-384, 34 Stat 768 (1906).

¹⁴⁶ Van Tassel, 6 Ind Health L Rev at 230 (cited in note 116).

¹⁴⁷ Michelle Meadows, *A Century of Ensuring Safe Foods and Cosmetics*, FDA Consumer Magazine, The Centennial Edition (Jan–Feb 2006), online at <http://www.fda.gov/AboutFDA/WhatWeDo/History/FOrgsHistory/CFSAN/ucm083863.htm> (visited Sept 15, 2013).

contain a single strawberry.¹⁴⁸ It was made of highly carcinogenic coal tar, artificial chemical pectin, artificial chemical flavorings, grass seeds, and other chemical preservatives.¹⁴⁹ Consumers had no way to learn of this poor quality, as ingredients were not listed on labels.¹⁵⁰ This information asymmetry meant that consumers were not able to engage in self-protection.

This period of time also saw a remarkable growth in the marketing of sham products to treat and cure disease.¹⁵¹

During this long period in U.S. history, the curative claims of predatory sham medicine salesmen were limited only by the gullibility of their targets. In many cases, the degree of gullibility was proportional to the level of desperation of the individual for a cure. The more dire the condition, the more vulnerable an individual was to the “flim flam” of the greedy snake oil salesman. And the more dire the condition, the greater the degree of harm when the sham medicine did not work, causing injury over and above the original illness and/or causing a delay in seeking effective medical treatment.¹⁵²

To address both of these problems, Congress passed the 1938 Food, Drug, and Cosmetic Act (“1938 Act”), which is still in force today. The 1938 Act answered the question of the proper regulatory balance between the protection of individual choice in matters involving self-regarding behavior, such as choosing a consumer product or medicine, and the need to protect vulnerable consumers from harm from third parties. The 1938 Act created this balance by linking the level of product regulation with the level of vulnerability of the product’s targeted population. This linkage translates into the provision of the greatest amount of regulatory protection when products are targeted at vulnerable populations. This linkage also established the proper balance between regulating to protect public health while allowing innovation to flourish.

¹⁴⁸ Id.

¹⁴⁹ Id.

¹⁵⁰ Id.

¹⁵¹ Van Tassel, 6 *Ind Health L Rev* at 219–24 (cited in note 116).

¹⁵² Id. at 216–17.

1. Regulating to protect vulnerability created by ill-health.

The FDCA of 1938 identifies two types of vulnerability. The first is vulnerability that is created by ill health. Thus, products claiming to aid in an individual's struggle to return to normal health fall into the categories of products that require the greatest amount of regulation. Examples of products that fall into this category include drugs and devices that require premarket approval.¹⁵³ This places the burden of proving both safety and effectiveness on the manufacturer before these products can be placed on the market.¹⁵⁴ Thus, the 1938 FDCA sharply curtailed the ability of the quack salesman to take advantage of the desperation of those who suffer from ill health.

On the other hand, the FDCA requires far less regulatory protection when products are targeted to healthy populations to *maintain or improve* a normal state of health—for example, dietary supplements or functional foods.¹⁵⁵ Less regulation is needed as this group of consumers is not blinded by desperate desires to cure unbearable illnesses and return to good health.

Finally, the FDCA requires the least amount of regulation to protect consumers in the context of traditional food. There is little need to provide regulatory protection for consumers in this context

as thousands of years of use of traditional food provides consumers with the common knowledge, and thus the ability, to protect themselves from the ordinary risks associated with different traditional food products. . . . This common knowledge and ability to self-protect supports the presumption of safety that is granted to traditional food under the FDCA.¹⁵⁶

Therefore, traditional food products can be placed directly on the market without undergoing any testing for safety.¹⁵⁷

¹⁵³ 21 USC § 355(a) and 28 USC § 360e, respectively.

¹⁵⁴ Van Tassel, 6 Ind Health L Rev at 236–41 (cited in note 116).

¹⁵⁵ Id. The term “traditional food” is used to distinguish this category of product from genetically modified food.

¹⁵⁶ Id at 230.

¹⁵⁷ Id at 230–31. Therefore, if a particular food poses a safety risk over and above those which are normally associated with a food product, such as salmonella in peanut butter, the FDA carries the burden of proving that the food is adulterated or misbranded before it can be removed from the market. Id.

With these second two categories, the FDCA assumes that consumers can engage in self-protection based on common, customary knowledge regarding the risks associated with these products. Of course, with regard to dietary supplements, this assumption is suspect as many contain biologically active ingredients that are being newly introduced into US markets.

2. Regulating to protect vulnerability created by information asymmetry.

In addition to recognizing and protecting consumer vulnerabilities relating to ill-health, the 1938 Act also recognized a second kind of vulnerability that occurs when there is an information asymmetry between the manufacturer of a product and the consumers that the product targets. For example, in order to cure the asymmetry created by the processed food revolution, the FDCA required that the ingredients of a food product be listed on the label. A good example of information asymmetry in the processed food context is the black box that was created by the advent of canned stews with unknown contents. The FDCA's listing cure worked for traditional food product ingredients that were contained in these canned stews, such as tomatoes and potatoes, as the health risks associated with these ingredients were common knowledge.¹⁵⁸ With this ingredient listing, consumers who had a history of an allergic or toxic reaction to a particular traditional ingredient could engage in self-protection by avoiding the product. Enabling consumers to engage in self-protection created the first line of defense that makes up the first part of the public health product safety net.

¹⁵⁸ See *id.*, explaining that "The 1938 Act eliminated the 'distinctive name proviso' and required instead that the label of a food 'bear its common or usual name.' The food would be illegal or misbranded if it represented itself as a standardized food unless it conformed to that standard." Meadows, *A Century of Ensuring Safe Foods and Cosmetics* (cited in note 147). The FDCA authorized three kinds of food standards—identity, quality, and fill of container. *Id.* In 1939, the first food standards were issued for canned tomatoes, tomato purée, and tomato paste. *Id.* The standards looked like a recipe of listed ingredients. *Id.* The next standards were for jams and jellies. "By 1957, standards had been set for many varieties of foods such as chocolate, flour, cereals, bakery products, milk, cheese, juices, and eggs." *Id.*

C. Novel Ingredients and the Food Additives Amendments of 1958

Unfortunately, the 1938 Act did not anticipate the creation of hundreds of novel chemicals for the use in processed foods during the 1930s through the 1950s. Unlike the listing of common traditional foods, such as tomatoes and potatoes, the listing of these novel ingredients on food labels did nothing to help consumers deal with these novel ingredients, as no common knowledge existed regarding their health risks.¹⁵⁹ By the 1950s, the popular movement to regulate these chemical food additives slowly gained traction and ultimately led to passage by Congress of the Food Additives Amendment of 1958.¹⁶⁰ The Food Additives Amendment placed the burden on the chemical additive industry to establish the safety of novel chemicals through premarket testing for safety. Significantly, as the next two subsections explain, this testing only decreased the uncertainty over any possible health risks to a small degree for average consumers and almost not at all for idiosyncratic consumers.¹⁶¹ The question then became how to deal with this excess uncertainty. The answer, as explained in the next sections, was the creation of what this Article calls the public health product safety net.

¹⁵⁹

In 1950, the Delaney Committee started a congressional investigation of the safety of additives that laid the foundation for the Food Additives Amendment and the Color Additive Amendments. Rep. James Delaney, D-NY, later submitted a change to the bill proposing the Food Additives Amendment by inserting the Delaney Clause, which prohibited the approval of any food additive shown to induce cancer in humans or animals in studies with a relevant route of exposure. Variations of the Delaney Clause were also included in the Color Additive Amendments and animal drug provisions.

Id.

¹⁶⁰ Id.

¹⁶¹ Id, explaining that

Enacted in 1958, the Food Additives Amendment required manufacturers of new food additives to establish their safety to FDA's satisfaction before marketing. Food additives are substances that have no proven track record of safety and that must be approved by the FDA before they can be used. A food substance generally recognized by qualified experts as safe (GRAS) for its intended use, based on publicly available information, is excluded from the definition of food additive. Also in 1958, the FDA published the first list of GRAS substances, which contained nearly 200 substances including ascorbic acid, papain, and propylene glycol.

1. Excess uncertainty regarding health risks: premarket testing and predictability of health risks for average consumers.

As a general matter, premarket safety testing required by the FDCA involves studies that use very small sample sizes.¹⁶² These small sample sizes mean that the uncertainty over the possibility of health risks from exposure to novel ingredients is decreased to only a certain degree by premarket testing, leaving a significant excess amount of uncertainty.

For example, similarly small sample sizes with relatively low statistical power are relied upon to test safety and effectiveness for drugs today.¹⁶³ The FDA recognizes that these drug studies are too small to predict a large portion of the health risks associated with novel substances. However, as larger, more statistically powerful studies are deemed too expensive, the FDA regularly approves novel drugs with the understanding that the only way to seriously decrease the excess uncertainty over safety is to expose the drug to the genetic diversity of the general population.¹⁶⁴ The FDA then uses the post-market surveillance system specially created for drugs and medical devices to collect health data over time relating to the long-term exposures of the population to these novel chemicals to fully identify the statistical probability of adverse reactions.¹⁶⁵ Under this premarket testing regime, to date, serious adverse effects were not detected for approximately one-half of the drugs on the market until after the drugs received regulatory approval and were made available to the general population.¹⁶⁶ Discovering these serious adverse side-effects has led to many drugs and medical devices being pulled from the market as the information

¹⁶² Shelby D. Reed, et al, *Use of Larger Versus Smaller Drug-Safety Databases Before Regulatory Approval: The Trade-Offs*, 27 Health Aff 360, 360–61 (2008).

¹⁶³ Id.

¹⁶⁴ Id. See also Marshall S. Shapo, *Experimenting with the Consumer: The Mass Testing of Risky Products on the American Public* (Praeger 2008) (providing an excellent discussion across a wide range of products of how manufacturers of new products fail to disclose potential risks—or uncertainties about danger—to consumers who then become unwitting experimental subjects when products are first introduced into the market).

¹⁶⁵ Kevin Bullis, *Screening for Toxic Nanoparticles: Researchers Suggest a Strategy That Could Weed Out Dangerous Nanoparticles*, Tech Rev (Feb 7, 2006), online at <http://www.technologyreview.com/news/405268/screening-for-toxic-nanoparticles/> (visited Sept 15, 2013).

¹⁶⁶ Reed, 27 Health Aff at 366–67 (cited in note 162).

gathered from post-market monitoring has demonstrated that their actual risks outweigh their benefits. In the case of some other drugs and medical devices, the discovery of serious side-effects have led to the addition of safety measures, such as warnings, when it is discovered over time that their actual risks, though serious, are still outweighed by their potential benefits. Thus, there is a regulatory recognition that premarket testing will not detect many adverse reactions when novel substances are distributed to the general population for use as drugs. The bottom line is that post-market monitoring of novel substances protects public health by managing the uncertainty over health risks that premarket testing cannot significantly diminish.

For example, news of new and serious risks associated with FDA-approved drugs is common.¹⁶⁷ A readily recognized example is the case of Vioxx.¹⁶⁸ Subsequent to FDA approval, distribution to over 2 million people in the United States, and marketing to 80 different countries for total sales of 2.5 billion dollars, it was discovered that Vioxx increased the risk of heart attack and stroke by 50 percent.¹⁶⁹ Another more recent case is that of Omontys, a drug approved by the FDA in March of 2012 to treat adult patients on hemodialysis with anemia stemming from chronic kidney disease.¹⁷⁰ This approval was based upon a relatively large premarket approval study, after which an FDA advisory panel endorsed the drug by a vote of 15–1.¹⁷¹ The chair of the panel remarked that the drug “doesn’t have any safety signals.”¹⁷² Only one year later, in February of 2013, based on data gathered from post-market surveillance, the FDA warned of serious and fatal reactions to Omontys and counseled that physicians should discontinue its use in all patients immediately.¹⁷³

¹⁶⁷ Id.

¹⁶⁸ Rita Rubin, *How Did Vioxx Debacle Happen?*, USA Today (Oct 12, 2004), online at http://usatoday30.usatoday.com/news/health/2004-10-12-vioxx-cover_x.htm# (visited Sept 15, 2013).

¹⁶⁹ Id.

¹⁷⁰ John Gever, *Fatal Reactions Prompt Omontys Recall*, Medpage Today (Feb 24, 2012), online at <http://www.medpagetoday.com/HematologyOncology/Anemia/37509> (visited Sept 15, 2013).

¹⁷¹ Id.

¹⁷² Id.

¹⁷³ Id.

Just as is the current situation with drugs, chemical preservatives and flavorings were tested under the Food Additive Amendments Act of 1958 using small sample sizes with the understanding that these studies could only identify a portion of these novel chemical's adverse effects. Those that were approved were added to food and distributed to the general population. As with novel drugs and the current post-market surveillance system set up by the FDA, the public health product safety net came into play when novel chemical food additives were approved based on premarket testing which only partially decreased the uncertainty over the associated health risks. This safety net was activated by the simple, but essential, step—the requirement that novel ingredients be listed on a product's packaging.

Activating the safety net started with the FDA's recognition of the fact that the *novelty* of these chemicals meant that their addition to food was "material" because neither the manufacturers nor the FDA knew what the actual risks of exposure to these novel ingredients would turn out to be, in spite of premarket safety testing. Under the 1938 Act, the material nature of the new ingredients meant that consumers were required to be given notice so that they would not assume that the nature of the risk was the same as the traditional food products without the novel chemical additives.¹⁷⁴ In order to give consumers notice, these novel chemical ingredients were required to be listed on the product labels. Listing activated the first line of safety by allowing the consumer to engage in self-protection. Then, if the consumer experienced an injury through exposure to a product, that consumer could search the label and identify the novel ingredient and avoid it in the future. If the injury was serious enough to warrant a trip to the doctor, because the consumer could identify the causative agent, proper treatment could be provided, minimizing the cost of treatment, the extent of the injury, and the time for recovery. The physician could then accurately report the injury and its cause to the public health officials of the appropriate state or federal agency. If the cumulative data suggested that the product was unsafe, the early warning and recall mechanisms could be used by the public health officials of the state or federal agency to avert a

¹⁷⁴ See notes 101 and 102.

public health crisis. This data could also be used to meet the evidentiary requirements of the tort system, allowing it to be used instrumentally to increase product safety.

2. Excess uncertainty regarding health risks: premarket testing and predictability of health risks for idiosyncratic consumers.

More seriously, the initial studies performed during the premarket approval process to decrease some uncertainty for the average consumer, provide little to no assurance for those who are referred to by the law as the “idiosyncratic consumers” or non-average consumers.

The premarket studies required by the FDA are simply too small to say much about safety for those who are not average.¹⁷⁵ These consumers must rely 100 percent on self-protection by watching ingredients listed on labels and stopping exposures to novel ingredients as soon as they are symptomatic. Or, in relation to long-term exposures, by hoping the public health product safety net will be sensitive enough to pick up a surge in injuries relating to novel products so that public health agencies can issue a recall of that product. So, with novel ingredients, the only way to significantly decrease uncertainty over health effects for idiosyncratic consumers is to distribute the product to the general population. Then, public health officials must “wait and see,” while, at the same time, hoping to catch early warning signs of a serious problem in time to minimize injuries through early warnings and product recalls.

D. In the Past, a Focus on Novelty Created the Public Health Product Safety Net to Deal with Uncertainty Over Health Risks

To recap, this history explains the overall FDCA regulatory scheme that makes regulatory choices by balancing the protection of individual choice in matters involving self-regarding behavior, such as choosing a consumer product, with the need to protect vulnerable consumers from harm from third parties. This balance is created by linking the level of product regulation with the nature and level of vulnerability of the

¹⁷⁵ See Reed, 27 Health Aff at 366–67 (cited in note 162).

product's targeted population. This linkage translates into the provision of the greatest amount of regulatory protection when products are targeted at the most vulnerable populations.

Vulnerability can arise in two basic ways. First, vulnerability can arise in situations where products are targeted to those with ill health. The FDA ensures that product manufacturers cannot take advantage of this vulnerability, as was the case with predatory snake oil salesman, by requiring premarket testing to ensure that the product is actually as effective as claimed. On the other hand, for products that are targeted to the healthy population, vulnerability can arise because of information asymmetries between the manufacturer of a product and the consumers that the product targets. The FDA cures this second type of asymmetry by requiring that all of the information that is material to a reasonable consumer is listed on the label. History shows that one type of information asymmetry that creates a consumer vulnerability is when *novel* ingredients are not listed on labels. Without this information, consumers can't engage in self-protection—just like when canned stews with novel chemical preservatives and flavorings were first introduced.

The FDCA dealt with novel chemical food additives and consumer vulnerability arising out of their unknown health risks by requiring premarket testing to decrease some of the uncertainty over health risks. However, this testing still left a great deal of remaining uncertainty. The FDCA dealt with this remaining uncertainty by acknowledging that this uncertainty was material and, therefore, requiring ingredient listing in order to enable the public health product safety net. This safety net was, and still is, used to capture signals that indicate that a product may cause injury to health in order to avoid, or at least mitigate, harm to all consumers through early warnings and product recalls

The next section describes how this precedent should be used to regulate the novel, innovative ingredients of today and tomorrow.

IV. ANIMATING THE PUBLIC HEALTH PRODUCT SAFETY NET TO CAPTURE CONSUMER PRODUCTS THAT USE INNOVATIVE TECHNOLOGIES

As it did with novel chemicals in the 1950s, the focus on *novelty*¹⁷⁶ rather than *hazard* in the context of nanotech ingredients takes the analysis out of the realm of scientific uncertainty and empowers the FDA to regulate nanotech consumer products to protect public health. A focus on novelty acknowledges that the public health product safety net plays a critical role in the identification of unsafe products in the context of both products that have gone through premarket testing and, importantly, those that have not.

A. Information Vulnerability and Novel Ingredients

The recognition that the vulnerability in the case of novel ingredients, for example nanotech ingredients, is related to an information asymmetry and that this asymmetry is material has a domino effect that results in animating the powerful public health product safety net. The only step the FDA needs to take in order to engage the public health product safety net is to recognize that the failure to list a novel ingredient, such as a nanotech component, is a “material” omission under the FDCA. In order for this omission to be “material,” it must be “misleading.”¹⁷⁷

¹⁷⁶ One way to define novelty is to track the way this term is defined by the European Union in the context of dietary supplements: “European Union novel foods require any food or ingredient that can’t demonstrate a history of use prior to May 1997 to verify its safety and intended use.” Shane Sterling, *Consultant: ‘No Need to Fear EU Novel Food Laws’*, NutraIngredients.com (William Reed Business Media Apr 29, 2013), online at <http://www.nutraingredients.com/Regulation/Consultant-No-need-to-fear-EU-novel-foods-laws> (visited Sept 15, 2013). Another possibility is to link the definition to the substances that are subject to a patent.

¹⁷⁷ See text accompanying note 102 explaining that, under the FDCA, a drug, device, food, dietary supplement, cosmetic, or sunscreen is deemed misbranded if its labeling is “false or misleading in any particular.” 21 USC § 362(a) (2006). See also 21 CFR § 701.1 (2011).

[I]n determining whether the labeling or advertising is misleading . . . there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article.

21 USC § 321(n) (2009).

As described in the next section, there are several compelling arguments that this information asymmetry created through intentionally omitting to list novel, innovative ingredients is misleading. If the omission is misleading, this creates an information defect that renders the product misbranded. If the product is misbranded, it cannot be distributed to consumers.

1. Intentionally failing to list novel, innovative ingredients is materially misleading, rendering the product misbranded.

To put the analysis of “materiality” into a real world context, the ingredient lists on nanotech products currently refer to the host product’s nanotech content by the same name as the ingredient’s normal size counterpart. For example, the use of nanotech titanium dioxide is so ubiquitous in sunscreens as to be almost unavoidable. Instead of this nanotech titanium dioxide content being listed as “nano titanium dioxide,” as is required by law in the European Union,¹⁷⁸ manufacturers in the United States just list this ingredient as they always did before they started using the nanotech version of this chemical—it is listed as “titanium dioxide.” Thus, manufacturers in the United States are allowed to hide their products’ nanotech ingredient content from consumers.

This practice is misleading for numerous reasons. First, when consumers choose to use a new product for the first time, and they are aware that they are using a new product, they engage in self-protection by being more vigilant in watching for any untoward effects. This is particularly true for parents of small children, those who suffer from ill health, and those who deal with multiple allergies. When manufacturers misrepresent¹⁷⁹ to consumers that the ingredient is a normal

¹⁷⁸ Iris Eisenberger, et al, *On Voluntary and Obligatory Nano-Labeling*, 31 Nano Trust Dossiers 1 (July 2012), online at http://epub.oew.ac.at/Oxc1aa500d_0x002c9d9a.pdf (visited Sept 15, 2013) (providing publication of the Institute of Technology Assessment of the Austrian Academy of Sciences explaining the European Union requirements for labeling nanotech cosmetics and food and summarizing the status of the labeling movement among EU countries).

¹⁷⁹

One who fraudulently makes a misrepresentation of fact, opinion, intention or law for the purpose of inducing another to act or to refrain from action in

size ingredient, the consumer will likely have been exposed to this normal size ingredient in the past. If this past exposure has not caused any harm, the consumer will assume that the need for self-protection through heightened vigilance is unnecessary. Thus, the consumer's natural self-defense mechanism will have been disarmed by the manufacture's misrepresentation.

The second reason that this practice is misleading is that, if a consumer has a negative physical reaction to the nanotech ingredient (which the current state of the science suggests is possible, even likely),¹⁸⁰ the consumer will be unaware that the adverse reaction is to the novel ingredient. Instead, the consumer will assume that the injury was caused by the host product and will avoid that product in the future. If, for example, the product is a sunscreen containing unidentified nanotech titanium dioxide and nanotech zinc oxide, this incident may cause the consumer to incorrectly believe that they can no longer use sunscreens at all. This results in an unnecessary avoidance of a product that could protect the consumer from other serious health consequences such as skin cancers, a category of diseases that includes malignant melanomas, which have a rapidly increasing incidence rate over the past several years as a result of current problems with the ozone layer.¹⁸¹

The third reason that this deceptive practice is misleading is that, if a consumer has a negative physical reaction to the nanotech ingredient, the consumer will rely upon the proper listing of ingredients on product labels in order to provide their physicians with an accurate list of exposures so that they can be correctly diagnosed and treated. A simple but very common example occurs when a consumer develops a rash. In determining the proper treatment, one of the first questions that a physician is likely to ask is whether the consumer/patient has purchased any new products for regular use. In other words,

reliance upon it, is subject to liability to the other in deceit for pecuniary loss caused to him by his justifiable reliance upon the misrepresentation.

Restatement (Second) of Torts § 525 (1977). "A misrepresentation is material if it would be likely to induce a reasonable person to manifest his assent, or if the maker knows that it would be likely to induce the recipient to do so." Restatement (Second) of Torts § 162 (1965).

¹⁸⁰ See notes 70–94 and accompanying text.

¹⁸¹ Doris Day, *As Cancer Deaths Fall, Malignant-Melanoma Rates Rise*, LiveScience (June 3, 2012), online at <http://www.livescience.com/37124-skin-cancer-deaths-grow.html> (visited Sept 15, 2013).

whether there are any new exposures that could be the cause for the rash. A misleading label will thwart the physician's ability to determine the cause of the rash in order to properly treat the condition.

The fourth reason this practice is misleading is that individual consumers assume that the public health product safety net is fully engaged and that, if the product is unsafe, the early warning and product recall system will warn them to avoid the product if it is causing harm. Parents with small children, those who suffer from ill health, and those who deal with multiple allergies are particularly reliant on these product warning and recall systems. As both the consumer and the physician have no idea that the consumer has been exposed to the novel nanotech ingredient, neither can properly report the injury to any to the state or federal agencies that collect and analyze the data that is relied upon to alert the public of unsafe products through early warning and product recall systems.

The fifth reason this practice is misleading is that consumers purchase products with the customary understanding that, if the product is unsafe and a consumer is injured, the manufacturer will compensate them for these injuries. As explained earlier, the failure to list nanotech ingredients on product labels means that manufacturers of nanotech ingredients are insulated from tort recovery. Consumers have no notice of this special immunity and, consequently, are not aware that the product carries a special risk as the consumer won't be compensated for any injuries the product causes.

These arguments support a finding that novel, innovative ingredient content in a consumer product is information that is material to a consumer making a choice over whether to use a consumer product. Failure to provide material information renders a product misbranded, violating the FDCA.

B. Application to Future Technologies

This focus on novelty will engage the public health product safety net to provide post-market surveillance for novel ingredients created by the new technologies of the future. Thus, as the food is created and placed on the market using meat from

cloned animals,¹⁸² or meat grown in the lab,¹⁸³ or through the genetic modification of animals,¹⁸⁴ the FDA can regulate to protect public health in a way that minimizes the roadblocks to innovation. It is interesting to note that, if genetically modified plants used for food had been identified as such pursuant to an FDA focus on novelty, it is likely that much of the controversy over its possible health effects would have abated as the public health product safety net is likely to have picked up any short term allergic or toxic reactions.¹⁸⁵

¹⁸² Food and Drug Administration, *Animal Cloning*, online at <http://www.fda.gov/animalveterinary/safetyhealth/animalcloning/default.htm> (visited Sept 15, 2013).

¹⁸³ People for the Ethical Treatment of Animals, *PETA Offers \$1 Million Reward to First to Make In Vitro Meat*, online at <http://www.peta.org/features/In-Vitro-Meat-Contest.aspx> (visited Sept 15, 2013); Julieanne Strachan, *From a Petrie Dish to Your Plate*, ACT News (June 12, 2012), online at <http://www.canberratimes.com.au/act-news/from-a-petrie-dish-to-your-plate-20120602-1zpaau.html> (visited Sept 15, 2013).

¹⁸⁴ Food and Drug Administration, *Genetically Engineered Animals*, online at <http://www.fda.gov/animalveterinary/developmentapprovalprocess/geneticengineering/geneticallyengineeredanimals/default.htm> (visited Sept 15, 2013).

¹⁸⁵ From the outset, food manufacturers using genetically modified (“GM”) ingredients have declined to provide consumers notice of GM content. The FDA has not mandated disclosure as it takes the position that the introduction of GMO ingredients into food is not material. See generally Katharine Van Tassel, *Genetically Modified Food, Risk Assessment and Scientific Uncertainty Principles: Does the New Understanding of the Networked Gene Trigger the Need for Post-Market Surveillance to Protect Public Health?*, 15 BU J Sci & Tech L 250 (2009); Stephanie Strom, *Genetic Changes to Food May Get Uniform Labeling*, NY Times (Jan 31, 2013), online at http://www.nytimes.com/2013/02/01/business/food-companies-meet-to-weigh-federal-label-for-gene-engineered-ingredients.html?pagewanted=all&_r=0 (visited Sept 15, 2013). This lack of transparency resulted in consumer rights groups testing products for GMO use and disclosing that use to consumers. Non GMO Project, *GMO Facts: Frequently Asked Questions* (Non-GMO Project 2013), online at <http://www.nongmoproject.org/learn-more/> (visited Sept 15, 2013). As consumers have become aware of the extensive use of GMOs in their food, a rising number have expressed the desire that these ingredients be labeled. Rachel Hennessey, *GMO Food Debate In The National Spotlight*, Forbes, (Nov 3, 2012) online at <http://www.forbes.com/sites/rachelhennessey/2012/11/03/gmo-food-debate-in-the-national-spotlight/> (visited Sept 15, 2013) (“70% of items in America’s grocery stores contain genetically modified organisms”). A recent ABC poll suggests that 93 percent of consumers now support mandatory disclosure of GMO content on labels. Gary Langer, *Poll: Skepticism of Genetically Modified Foods*, ABC News (June 19, 2012), online at <http://abcnews.go.com/Technology/story?id=97567&page=1> (visited Sept 15, 2013). When the industry ignored the consumer preference for listing of GM content, a market was created for products that are “GMO-free.” Thus, the practice of “GMO-free” labeling was born. The growing consumer labeling movement also triggered repeated attempts to pass labeling laws. While these efforts have been unsuccessful to date, they are gaining traction—for instance, it cost the industry 40 million dollars to block California’s Proposition 37 calling for mandatory labeling last fall. Strom, *Genetic Changes to Food*, NY Times (cited in note 185). With more legislative proposals cropping up (a ballot initiative in Washington state and legislative proposals in Connecticut, Vermont, New Mexico, and Missouri), a growing consumer boycott of some organic or “natural” brands owned by major food companies and a recently introduced popular

V. DOES COST-BENEFIT ANALYSIS BAR THE LISTING OF NOVEL INGREDIENTS ON PRODUCT LABELS?

Every president since Richard Nixon has established a program to require review and clearance of agency regulatory decisions before they are placed into effect.¹⁸⁶ Usually, this review is conducted by the Office of Information of Regulatory Affairs (OIRA), which is part of the Office of Management & Budget (OMB), using cost-benefit analysis.¹⁸⁷ Cost-benefit analysis

mobile app by Fooducate that allows consumers to check for GMO content in a growing number of products, industry may be seeing the writing on the wall. Id; Hank Schultz, *Popular Mobile Food App Adds GMO Feature*, FOODnavigator-usa.com (Oct 17, 2012), online at <http://www.foodnavigator-usa.com/Business/Popular-mobile-food-app-adds-GMO-feature> (visited Sept 15, 2013). Just this year, Ben & Jerry's Ice Cream has decided to remove GMO ingredients from its supply chain. Hank Schultz, *Research Results Pointed Ben & Jerry's Down Non-GMO Path*, FOODnavigator-usa.com (Feb 1, 2013), online at <http://www.foodnavigator-usa.com/Business/Research-results-pointed-Ben-Jerry-s-down-non-GMO-path> (visited Sept 15, 2013). And the Meridian Institute, which organizes discussion of major issues, convened a meeting in Washington just last month that included executives from PepsiCo, ConAgra, and about 20 other major food companies, as well as Wal-Mart and advocacy groups that favor labeling. Strom, *Genetic Changes to Food* (cited in note 185). Just in March of 2013, three major grocery chains announced that they will require food with genetically modified ingredients to list these innovative ingredients on product labels. Stephanie Strom, *Major Grocer to Label Foods With Gene-Modified Content*, NY Times (March 8, 2013), online at <http://www.nytimes.com/2013/03/09/business/grocery-chain-to-require-labels-for-genetically-modified-food.html?pagewanted=all> (visited Sept 15, 2013). Many are predicting that voluntary labeling may be right around the corner.

¹⁸⁶ Dana D. Dana, *Bad for Democracy: How the Presidency Undermines the Power of the People* 152–53 (Minnesota 2008) (discussing the increasing presidential power pursuant to the theory of the unitary executive that promises undivided presidential control of the executive branch and its agencies as well as expanded unilateral powers).

¹⁸⁷ See Office of Management and Budget, *Circular A-4* (September 17, 2003), online at http://www.whitehouse.gov/omb/circulars_a004_a-4 (visited Sept 15, 2013):

In theory, cost-benefit analysis of a policy option enumerates all possible consequences, both positive and negative; estimates the probability of each; estimates the benefit or loss to society should each occur, expressed in monetary terms; computes the expected social benefit or loss from each consequence by multiplying the amount of the associated benefit or loss by its probability of occurrence; and computes the net expected social benefit or loss associated with the government policy by summing over the various possible consequences. The reference point for these calculations is the state of the economy in the absence of the government policy, termed the “baseline.”

Nicholas A. Ashford, *The Legacy of the Precautionary Principle in US Law: The Rise of Cost-Benefit Analysis and Risk Assessment as Undermining Factors in Health, Safety and Environmental Protection*, in Nicolas de Sadeleer, ed, *Implementing the Precautionary Principle: Approaches from the Nordic Countries, EU and USA* 352, 366–67 (Routledge 2007). Cost-benefit analysis attempts to describe the consequences of a candidate regulation in monetary terms. This poses two problems. One is the difficulty,

is one of the primary tools used in regulatory analysis to anticipate and evaluate the likely consequences of rules. Although some regulatory benefits and costs are difficult to quantify or monetize, those preparing those analyses generally attempt to estimate the overall benefits that a proposed or final rule would create as well as the aggregate costs that it would impose on society, and then determine whether the former justify the later.¹⁸⁸

The first question becomes whether this cost-benefit tool should be used to judge any FDA regulations requiring the listing of novel ingredients on product labels? And, secondly, if this cost-benefit tool is used, appropriately or not, will such a regulation survive this process?

A. Is the Use of Cost-Benefit Analysis in the Context of Consumer Products and Individual Risk Appropriate?

How people react to scientific evidence of risk is governed by many factors, including how risk information is perceived and communicated, how individuals react to social and cultural influences, and how choices are structured.¹⁸⁹ Examples abound of situations where individuals' risk perceptions lead them to act in ways that appear contrary to their own interests, overreacting

even arbitrariness, of placing a monetary value on human life, health and safety, and a healthy environment. Another is that by translating all of these consequences into equivalent monetary units, discounting each to current value (since a US \$/Euro invested now is expected to earn interest over time), and aggregating them into a single US\$/Euro value intended to express the net social effect of the government policy, the effects on the economy from investing now in future health, safety, and environmental benefits are weighted far more heavily than those benefits that occur in the future, including those to future generations.

¹⁸⁸ Id. For an excellent critique of the role of OIRA, its use of cost-benefit analysis, and suggestions for modification of OIRA's role, see John S. Applegate, et al, *Comments Regarding Executive Order on OMB Regularity Review*, Center for Progressive Reform (Mar 16, 2009), online at http://www.reginfo.gov/public/fjsp/EO/fedRegReview/CPR_Comments_New_EO_Reg_Rev_Final.pdf (visited Sept 15, 2013) (pointing out that the use of cost-benefit analysis by OIRA is inconsistent with the law in most cases and explaining how it is a failed tool of regulatory analysis).

¹⁸⁹ See generally Cass R. Sunstein, *Laws of Fear—Beyond the Precautionary Principle* (Cambridge 2005) (analyzing the relationship between “fear,” danger, and the law); Richard A. Posner, *Catastrophe—Risk and Response* (Oxford 2004) (arguing that “realism about science and scientists, innovative applications of cost-benefit analysis, a scientifically literate legal profession, enhanced international cooperation, and a pragmatic attitude toward civil liberties are among the keys to coping effectively with catastrophic risks”).

to or neglecting risks.¹⁹⁰ Regardless of whether these choices are rational or not, when it comes to *individual risk*, as a general matter our society respects the choice of the individual to encounter or avoid a particular risk in accord with that individual's personal values.

In contrast, environmental risks are those faced by the collective population. In the context of *collective risk*, the question becomes how much risk the collective is willing to encounter, for example, in the air, water, and soil.¹⁹¹ Under our democratic system, one might suppose that the desired level of risk would be assigned by the voting public. Instead, the current use of cost-benefit analysis as a proxy for the collective will is an attempt to impose rationality into the decision-making process.¹⁹² Cost-benefit analysis disregards the will of the collective that may be driven by what some label as "irrational" perceptions of risk in light of the mathematical probability of that risk actually occurring.¹⁹³

Regardless of the merits of this sanitizing approach when it comes to *collective risk*,¹⁹⁴ it has no role in the area of consumer products and *individual risk*. With collective risk, the government is fulfilling its proper role in protecting individuals from the risks that arise from the activities of third parties

¹⁹⁰ Sunstein, *Laws of Fear* at 89–106 (cited in note 189).

¹⁹¹ Many strongly argue that this choice should be made in a democratic fashion. Nelson, *Bad for Democracy* at 150, 152 (cited in note 186) (noting that the inception of the series of presidential executive orders requiring review and clearance of agency regulatory decisions before they are placed into effect conducted by the Office of Management & Budget using cost-benefit analysis was a "significant turning point in the accumulation of presidential power, in the executive's receptiveness to business concerns, and in the diminished responsiveness of federal government to citizen interest").

¹⁹² Sunstein, *Laws of Fear* at 89–106 (cited in note 189).

¹⁹³ Id.; Posner, *Catastrophe* at 9–12 (cited in note 189). The question becomes whether collective choices that are driven by the values of individuals created by their life experiences should be pejoratively labeled as "irrational fear," a loaded term in American society that values "courage" and disparages the fearful. See John M. Kang, *The Burdens of Manliness*, *Harv J L & Gender* 477, 487, 490–507 (2010) (A stereotype exists that men, to be considered men, must prove that they are courageous. So embedded is the assumption that "[c]ourage and notions of manhood [are] inseparable, the very word for courage in many languages deriv[es] from the word for man."). Should these individual values be discounted or not counted at all through the use of cost-benefit analysis?

¹⁹⁴ For a collection of critiques of cost-benefit analysis from a wide variety of stellar academics, see Thomas O. McGarity, Sidney A. Shapiro, and David Bollier, *Sophisticated Sabotage: The Intellectual Games Used to Subvert Responsible Regulation* (Environmental Law Institute 2004).

when the individual has no ability to avoid the risk through their own initiative.¹⁹⁵ In contrast, in the context of consumer products and individual risk, the proper role of the government is to protect individual choice with regard to the amount and nature of the risk the consumer is willing to encounter.

B. What Result If Cost-Benefit Is Applied?

Even if the OMB inappropriately applies a cost-benefit analysis to a requirement that novel ingredients be listed on product labels, the benefits to public health far outweigh the costs. Thus, this FDA regulation is likely to survive this last OMB hurdle.

The cost of such a regulation will be *de minimus*. For example, the cost of placing two to four letters (“GM” or “nano”) in front of all novel, innovative ingredients listed on product labels is small. With regard to GM food, the old arguments that the majority of the cost lies in trying to maintain separate food collection and distribution systems so that GM versus GM-free food can be identified have become moot. The organic and GM-free movements have set up certification systems that require food producers and packagers to meet a set of strict requirements in order to be allowed to use the label denoting that their products are organic and/or GM free. Thus, the cost of keeping the GM-free food and GM food separated has been placed on the GM-free, natural food and is, thus, no longer relevant to the cost of the listing of GM ingredients in food.

The benefits of novel ingredient listing, as explained earlier, are the ability of a consumer to self-protect, to receive proper treatment if injured, and to allow for data collection and surveillance so that any uptick in injuries can be quickly detected and a crisis averted or mitigated. Finally, ingredient listing also allows for the data collection necessary for the tort system to work appropriately, which allows for compensation of injured parties and for the instrumental benefits of the tort system to accrue.

¹⁹⁵ Wickler, 56 *Health & Society* at 303–38 (cited in note 23).

VI. CONCLUSION

Currently, the litmus test the FDA uses to trigger regulation to protect public health when novel technologies are used to create innovative ingredients in consumer products is keyed to a finding of *hazard*. Linking public health protections to the degree of hazard when operating in scientific uncertainty is outcome determinative—it means no regulation at all. Thus, a focus on hazard translates into the FDA ignoring its prime mission, the protection of public health.

Instead, the FDA's lodestar for triggering regulation should be *novelty*. A focus on novelty results in the proper regulatory balance between the twin goals of fostering innovation while protecting public health. The results of this focus also fit well with the overarching theme of the FDCA that titers the degree and kind of regulation it uses to protect consumers from harm from third parties to the level and type of vulnerability of those consumers. It also tracks how the Act has historically dealt with regulating novel ingredients with unknown health risks by using what this Article calls the public health product safety net.

This safety net is created when the healthcare system, the state and federal public health protection agencies, and the tort system are all networked together to protect public health. This network is created through the simple expedient of novel ingredient listing. This one small step empowers consumers' abilities to self-protect, allows for appropriate medical treatment by the correct identification of harmful causative ingredients, and permits the proper reporting of products containing novel ingredients to the state and federal public health protection agencies in charge of the early warning and product recall systems. This data can then be collected to allow for the instrumental use of the tort system to encourage the proper investment in product safety by manufacturers and insulate against the overuse and overconsumption of relatively risky products by consumers. While this network is far from perfect, it is likely to improve exponentially as this country moves into the era of big data and the collection of product safety information reported directly by consumers in social media.

The proposed regulation of the use of nanotechnology in consumer products set forth in this Article provides a good example of how regulation based on *novelty* rather than *hazard*

achieves the proper balance between protecting public health while encouraging innovation through the animation of the public health product safety net. This same regulatory strategy should be applied to other novel technologies used as ingredients in consumer products such as cloned animals used for food, genetically modified plants and animals used for food, and lab grown meat.