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ORIGINAL PAPER

Beyond Implications and Applications: the Story of 'Safety by Design'

Christopher M. Kelty

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Abstract Using long-term anthropological observations at the Center for Biological and Environmental Nanotechnology in Houston, Texas, the article demonstrates in detail the creation of new objects, new venues and new modes of veridiction which have reoriented the disciplines of materials chemistry and nanotoxicology. Beginning with the confusion surrounding the meaning of 'implications' and 'applications' the article explores the creation of new venues (CBEN and its offshoot the International Council on Nanotechnology); it then demonstrates how the demands for a responsible, safe or ethical science were translated into new research and experiment in and through these venues. Finally it shows how 'safety by design' emerged as a way to go beyond implications and applications, even as it introduced a whole new array of controversies concerning its viability, validity and legitimacy.

Keywords Anthropology · Buckminsterfullerenes · Environmental engineering · Ethnography · Materials chemistry · Responsibility · Toxicology

C. M. Kelty (✉)
Department of Information Studies,
Center for Society and Genetics, UCLA,
Rolfe Hall 1323, Box 957221, Los Angeles,
CA 90095-7221, USA
e-mail: ckelty@ucla.edu

'Beyond Good and Evil.—At least this does *not* mean beyond good and bad.'[1]

There is evidence that 'buckyballs' are toxic to humans and the environment. And this might be a good thing. Before we might even object to such a claim, controversies emerge. What is a buckyball? What kinds of buckyballs, synthesized how, in what kind of solution? Pure or 'functionalized' (having molecular groups attached to the shell)? In aggregates or alone? Moving through an environment or body, or collecting there? Toxic to what? To cells, organs, animals, environments? Causing what kind of damage?

Between 2004 and 2007, the National Science Foundation Center for Biological and Environmental Nanotechnology (CBEN) at Rice University in Houston, Texas and an outgrowth of CBEN called the International Council on Nanotechnology (ICON) created new venues for defining what buckyballs (buckminsterfullerenes) are and what counts as toxicity. In the process developed new 'modes of veridiction' through which truth claims about safety and toxicity could be reconfigured as truth claims about the very nature of matter. As such, 'toxicity' was transformed from something that was the concern of those 'downstream' from chemistry or engineering into an engineerable property of new

[1] Nietzsche, *Genealogy of Morals,* first essay, section 17.

materials. This article, based in ethnographic research at CBEN from 2003 to 2008, explores how these new objects, venues and modes of veridiction came into being.

CBEN was originally funded (2001) to research the 'applications' of nanotechnology to environmental and biological issues, but quickly became embroiled in controversies around safety, risk, and concern for the responsible development of nanotechnology. Vicki Colvin, Mark Wiesner, Kristen Kulinowski, Kevin Ausman, Jennifer West, Rick Smalley and several others were closely involved in the creation of this new center and the definition of its research mission. From the beginning, Colvin and Wiesner argued at length (with each other and in public) over the definition of what the Center's core mission would be; later, with the help of Kulinowski (who was both executive director of CBEN and director of ICON), Colvin broadly communicated CBEN's mission, first under the label of 'Wow to Yuck?' and later under the label of 'Safety by Design' ([23]; cf. [35]). Because of the intense scrutiny that CBEN experienced based on its controversial research mission, members devoted more and more resources to the attempt to understand the 'implications' of nanotechnology. ICON, for example, was an outgrowth of CBEN (funded primarily by corporations and a supplementary NSF grant) intended to bring multiple stakeholders (government, corporate, academic, and civil society) together.[2] Its purpose was to explore the possibilities for pursuing responsible nanotechnology and communicating the risks and implications clearly.[3] Together these two new venues initiated research into the toxicity of buckyballs, transformed the meaning of the 'fundamental' properties of buckyballs and raised the question of who has the right and obligation to study them.

Scientists inside and outside of CBEN, especially nanotechnologists and materials chemists, had extremely hostile reactions to CBEN and its proposal to study risks to human health and the environment. They often claimed instead that the very research they proposed to do was a major risk to the health (i.e. funding and public acceptance) of nanotechnology as a viable discipline and research area. In response, CBEN and ICON argued that *not conducting* research on the health and environmental risks was what created the risk of public backlash, and which would be an even greater threat to nanotechnology research.

It was these two competing definitions of 'implications' that were eventually figured out by members of CBEN and ICON: risks to human and environmental health on the one hand, and risks to nanotechnology itself on the other.[4] This double meaning of 'implications' created confusion, but it was a kind of productive misunderstanding by which different problems and research questions could be distinguished. The language of 'implications' often inscribes a familiar distinction between a pure domain of nanotechnological investigation and an affected society in which there are unpredictable biological, environmental and social reactions to putatively basic research. But given the dual meaning of the term in this context, both the definition of what counted as pure science and what counted as the social, or non-scientific domain being affected, were undecided. Scientists and engineers from different backgrounds came to the project with different understandings. Materials chemists and those most earnestly calling themselves nanotechnologists defined CBEN's research in terms of applications designed to solve biological or environmental problems. Environmental engineers, toxicologists and some bioengineers, on the other hand, sought to put the study of implications on par with that of applications—to explore not only the fundamental *control* of matter, but fundamental *concern* about matter and its effects as well.[5]

In the midst of this controversy CBEN began to experiment with different approaches to the problem: the development of ICON and the idea of 'safety by

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[2] The story of the founding and transformation of CBEN and ICON is told in more detail in a related publication: [28].

[3] Initially, CBEN's budget included modest funding for social science (including for the research in this paper). As ICON and CBEN continued to call for more funding in this area, they became responsible for some of the momentum that led to the funding of the NSF Centers for Nanotechnology and Society in 2005.

[4] On the anthropological elaboration of 'figuring out' amongst actors in contemporary society, see [12].

[5] A word on the distinction between mode of concern and mode of control. The distinction has a fractal character, just as the distinction between basic science and implications does, depending on who is exercising the concern or the control. Kearnes [20] maps some of the ways that the language of 'control of matter' used in nanotechnology is always already a concern for particular values. In the story of safety by design, at issue is which kind of concerns, exactly, will be synthesized into a mode of control of matter: concerns over safety and risk, or concerns for energy efficiency, cost or profitability.

design' described in this article. When ICON was first created it seemed to be a way to channel the social issues—the issues of public perception and the threat to nanotechnology—away from and outside of the scientific core of CBEN. But what it achieved even more effectively was the channeling of questions about responsibility, implications, impact and society directly into the heart of scientific work funded by CBEN. The outcome of this arrangement is the story we tell here, the attempt to make 'safety' a fundamental property of new nanomaterials: 'safety by design.'

This article relies on anthropological methods and data to clearly demonstrate how this transformation came about—how the values being debated around 'implications' worked themselves into the very warp and weft of scientific and engineering activities and perhaps even into matter itself.[6] The demand in contemporary nanotechnology for an ethical approach, or even more generally for 'responsible science' [28] was in this case worked over through an array of techniques, governance structures, new venues and new metrics into something scientifically precise—*a mode of veridiction*. It became something that scientists and engineers could argue about (and vigorously) in a rarified and increasingly standardized language that maintains the quality of being value-neutral even as it expresses deeply held concern about consequences that are impossible to foresee.

The reason for the anthropological approach employed here is to unfold the process whereby these answers were reached, and the ramifications they have for the near future—and not only to report answers as they stand now. It has repeatedly been shown in the literature in history, philosophy and social study of science how 'science made' displaces 'science in the making.'[7] The work of stabilizing facts about the world is both experimental and rhetorical. In the case we offer here, we argue that it is all the more important to track and reveal this process of stabilization, not only in order to re-affirm the epistemological claims, but to demonstrate how, *and which*, values have now become embedded in the domain of nanotechnology.

This particular story of scientists at CBEN is far from generally true of nanotechnology—few other major centers of nanotechnology research have shown the kind of concern and creative re-evaluation of safety that CBEN has, and it remains a model to be emulated. However, the process described here, whereby value (in this case 'safety') is directly embedded in the experimental and theoretical work of science, is a more general process. We describe this process, following work by Rabinow and Bennett [34] on synthetic biology, as the creation of new venues within which shifting 'modes of veridiction' can come about and be tested, with ramifications for the very definition of new scientific objects (like buckyballs and their safety). Whether or not 'safety by design' will become a standard or an expectation in nanotechnology remains to be seen—but the possibility itself had to be painstakingly invented.

Can safety be a property of materials on par with other 'fundamental' properties like thermal conductivity, light absorption or stress/strain ratios? Based on this research, it is clear that what will count as fundamental is related to the definition of what counts as implications and what as basic science. In the case of nanotechnology, therefore, it is directly related to the fact that different scientific traditions, disciplines and communities are brought into contact.[8] In the story told here, the field of materials chemistry has been brought into direct connection with the environmental and biological sciences at the most basic level—akin to the role physics has historically played (and continues

[6] Anthropological research in this context includes long-term participant-observation amongst researchers in the centers and labs described here; telephone and in person interviews both formal (semi-structured and open ended) and informal (in the hallway or in offices); scrutiny of published and unpublished documents (research reports, grant proposals, documents used to coordinate and organize center research; and email correspondence) including reading and discussion of this paper and others at various stages. See [21] for a more extensive discussion of this method in nanotechnology.

[7] Latour [26] is the *locus classicus* for the claims about 'science in the making.' Cf. Melinda Fagan's recent work reconstructing the social context of stem cell research in order to demonstrate the alternate epistemological claims that can be made when one goes beyond simply the publications or textual claims [9, 10].

[8] Conventional terms in science studies that might describe 'safety by design' include boundary object' [40], boundary organization [16] or 'trading zone' [13, 14]—spaces within which intellectual differences, practical incompatibilities or linguistic translations are worked out. However, these concepts might not capture the specific re-working of values at stake in a case like the one presented here because they tend to emphasize the liminal space within which translations happens, and not the wholesale construction of new ways of distinguishing true and false within a discipline. A recent issue of *Perspectives of Science* reports on a related research into the origin and configuration of research in science. See [19, 29, 30]

to play) as the respected theoretical and experimental resource. But this 'bringing into connection' also has the power to remake some basic claims about matter. For instance, in classical chemistry, a new material like the buckminsterfullerene (C_{60}) is generally characterized with respect to properties measured and theorized in the idioms of physics: stress and strain, thermal and electrical conductivity, or molecular characteristics like solubility in water or strength of hydrogen bonds. Such are the established fundamental properties which nanotechnologists exploit in different ways in order to craft new materials with particular characteristics and implied uses (and on which successful nanotechnologists make their careers).

Defining 'safety' in similarly fundamental terms, however, requires bringing in concepts from biology and environmental science, such as oxidative stress, the response of cell membranes and their receptors, complex regulatory pathways, transport and degradation in marine and other ecologies and so on. These properties can also be exploited to craft new materials with implied uses. Hence the claim that buckyballs are toxic, but that this might be a good thing; given the right tools and experimental designs, toxicity can be tuned and controlled just as optical properties can be. Such a practice generates a new mode of veridiction in which claims about the safety of materials can be deemed true or false in new ways.

In the past, pioneers in nanotechnology have made their careers not primarily on the synthesis or discovery of materials but on the characterization of materials with respect to function. For example, the use of quantum dots for Light Emitting Diodes (LEDs) is generally associated with the work of Paul Alivasatos at UC Berkeley; similarly, the exploitation of carbon nanotubes for energy-related uses occupied much of Richard Smalley's research at Rice. It is precisely this 'career-making' aspect of the research which CBEN and Vicki Colvin have sought with the development of 'safety by design.' Safety becomes something whereby scientists can make new materials, make them safe and thereby make a career (or at least a legitimate and recognizable contribution) in nanotechnology.

Naturally, materials chemists' and nanotechnologists' careers are not the only ones at stake in such a move. Toxicologists, environmental scientists and engineers, biologists, as well as ethicists and social scientists have also sought to make names for themselves by studying the properties of new nanomaterials . The last four years have seen the emergence of both a field called 'nanotoxicology' ([32]; see also [25]) and one called 'nanoethics' [6], both arguably attempting to define and own some version of 'safety' in nanotechnology.[9]

For nanotoxicologists, for instance, 'safety' is not a property of materials, but a spectrum of (poorly understood) risks; environmental scientists and engineers, in addition, see this spectrum of risks as more than just a question of engineered materials, but one of complex ecosystems and subtle differences in the processes of manufacturing, disposing, and remediation of man-made materials. Most disagree on whether nanotechnology poses known or unknown risks, and have different opinions about and definitions of uncertainty; many would support a redefinition of their practices in terms of uncertainty rather than risk, but would do so in different ways [15].

At the heart of practical scientific activity therefore, the most detailed and novel debates about responsibility are taking place in idioms that on the surface seem to have little to do with those of ethics, regulation, or justice. But nor does the transformation of safety into a fundamental property occur simply because of the internal dynamics of scientific curiosity. Rather, in practically seeking new ways to become 'responsible' scientists actually *create a need* for responsible science—a new need that no previous configuration of sciences and disciplines claimed ownership over, and which can be filled (or fought over) as if it were the discovery of a *new scientific field*. Indeed, it is perhaps the only reliable manner through which responsibility will become practically 'doable'—by making it into something on which careers can be staked and towards which creativity can be channeled. Without such novelty, safety (and other forms of responsibility) are too easily seen as a

[9] The former is rooted firmly in a long history of work on ultrafine particles, including natural nano-scale particulate matter and its effect especially on pulmonary activity. It does not seek in any current form to create new materials or change the way materials are produced except insofar as it can demonstrate the toxicity of one kind of matter over another. The latter actively distances itself from environmental health and safety research as a domain that is distinct from properly ethical concerns, or concerns which nanoethicists worry are obscured by too heavy a focus on EHS research. This paper might then be seen as a kind of 'nanoethics of EHS research,' albeit one that claims to reveal 'ethics in the making' in the new venues of CBEN and ICON.

'downstream' and after-the-fact domain owned by no one, given over to consensus politics and treated as a bureaucratic issue (an iteration of the known with new variables) devoid of creative resolution or exploration.

Finally, this article does not argue for or against a particular version of safety. It should be understood instead as a 'characterization' (by analogy with the work of chemists who characterize new materials) of new venues, modes of veridiction and objects emerging in nanotechnology. The point of such an activity is to make it possible to articulate the values and the modes of argument being built into the near future of nanotechnology, in order to reflect in a grounded and empirically precise way, on the questions of ethics and responsibility which actually face us in concrete settings.

Carbon fullerenes (buckyballs), for instance, are not yet clearly defined as *objects*. Despite the ease with which scientists and science journalists refer to them as 'soccer-ball shaped molecules with sixty carbon atoms' the definition of carbon fullerenes is far from settled—whether or not they will be defined according to properties that include the environment and biology is as yet undetermined. Re-defining carbon fullerenes' fundamental properties in terms of safety could re-formulate everything from state regulation of materials to corporate marketing of them to standardization of their nomenclature. Not doing so will have similar ramifications.

Similarly, this story also demonstrates how new *venues* create a space for the incubation or filtering of values. ICON functions, metaphorically speaking, as a membrane to CBEN. It communicates CBEN's science to an unpredictable public, but it also receives, transduces and conducts the demand for responsibility into the cytoplasm and nucleus of experimental scientific work.

Finally, new *modes of veridiction* emerge—meaning simply that the criteria for true and valid scientific claims is reworked in these new venues and around these new objects. Whether buckyballs are 'toxic' is not a question that can be answered without specifying a few things about buckyballs as such. To cleave towards a definition given only in terms of number of atoms, strength of bonds, or shape permits no valid statement about toxicity; cleaving towards a definition given in terms of oxidation, free radicals, functionalization of the surface and mobility in different ecosystems, by contrast, permits a new set of truth claims to be made, challenged, defended and strengthened. Such claims can only be made by building new laboratories, recruiting new configurations of graduate students, and seeking money from unlikely places, or channeling it in ways it was not meant to be channeled. Object, venue and mode of veridiction therefore are interdependent in this story, and they are animated by a concern with making new things, making things safe, and thereby making new careers.

Fine Lines and Ultrafine Particles

Almost immediately after being funded, the Center for Biological and Environmental Nanotechnology (CBEN) found itself under intense scrutiny for their proposed research on the environmental and biological implications of nanomaterials. Even though they had designed the center to emphasize the 'applications' of nanotechnology to biological and environmental uses over the implications to environmental and biological health, there were both internal and external pressures on this configuration. Applications meant things like: membranes created with nanotechnology to filter polluted water (an 'enviromental application') or gold nanoshells used to treat cancer (a bioengineering application). Implications was fuzzier, but tended to mean concerns over FDA approval, environmental impact and toxicity and exposure studies. Internal to CBEN, there were tensions over whether implications research was properly scientific or not; externally there were corporations and civil society actors demanding more focus on the risks of new nanomaterials like C_{60} and carbon nanotubes. In reaction to this focus on implications, understood as risks to environment and biology, many nanotechnologists outside of CBEN began to focus on the risks to *nanotechnology itself*—also labeled 'implications'—that would emerge if scientists started talking about and investigating the former kind of risks.[10]

Fellow nanotechnologists, advisors, funders, deans and presidents, tried hard to silence two of the CBEN principals, Vicki Colvin and Mark Wiesner; they tried to prevent them from speaking about the need for such research, prevent them from being invited to

[10] See [28] for a detailed description of the founding of CBEN and the role of implications.

meetings, and at Rice University, held high-level meetings with the administration concerning how to reign in their promotion of such research. The anxiety over the potential de-funding of nanotechnology due to public backlash was fueled from many sources—fear and lack of understanding of 'the public'; popular misrepresentation in the press, novels and films; and a general consensus that one must logically develop positive applications before testing them for negative consequences. The double meaning of implications severely confused the debate: implications sometimes meant risks to human health and environment, and sometimes meant risks to nanotechnology of a public backlash and subsequent de-funding. Many human and social scientists also accepted this blurred meaning of implications, and have missed the opportunity, as Ebbesen [8] points out, to move beyond the issue of public acceptance.

CBEN principals exacerbated this confusion by giving frequent talks; Wiesner spoke often about not repeating the failures associated with DDT, Freon and Asbestos. Colvin and executive director Kristen Kulinowski developed the story of a 'Wow to Yuck?' trajectory of nanotechnology ([23, 24]; see also the analysis by [35]). By 2003, Colvin, Wiesner and executive director of CBEN, Kristen Kulinowski had given versions of their 'wow to yuck?' talk 'over two dozen times' to public audiences. Colvin had testified before congress in April of that year, had applied for 'supplemental funding' from the NSF for work on implications, and had begun to appear regularly on the roster of events as the keynote speaker who would address potential impacts of nanomaterials.

In October of 2003, Vicki Colvin published a 'perspectives' paper in *Nature Biotechnology* called 'The potential environmental impact of engineered nanomaterials' [4]. It was the first high-impact review of its sort, and was based primarily on the existing literature studying the toxicology, exposure and transport of ultrafine particles. CBEN had begun collecting and curating articles related to toxicological and environmental issues around 2003 in a database that would become the centerpiece of the work that ICON would do in 2004–5, and was eventually transformed into a 'virtual journal' highlighting specific articles in the area. Colvin's piece was based on these and rehearsed some of the basic issues of studying EHS: the need for understanding exposure as well as toxicity (such as occupational and manufacturing exposure and exposure through consumer products); the various systems for testing toxicity (human cell cultures, mouse fibroblasts, and animal models for pulmonary and neurological toxicology studies); issues of water-solubility and aerosolization and issues of free radical chemistry and anti-oxidation functions of new nanomaterials. The paper explicitly invokes the specter of a 'more skeptical and demanding public' that wants not only benefits but a commitment to 'anticipate and characterize potential risks' as well. It ends with a version of what had by then become the CBEN party line which combined the two kinds of implications, risks to human and environmental health, and risks to nanotechnology: 'Though it is challenging to assess the risks of engineered nanomaterials before commercial products are well defined, proactive research is critical to ensuring a sustainable nanotechnology industry (1169).'

Colvin's *Nature Biotechnology* paper fueled the existing fire of controversy around studying the implications of nanotechnology. For one thing, it made explicit the concern that no data exists—positive or negative—and so speculating about risks was unwarranted. But this was also Colvin's central message: without data, claims about the *safety* (or even the proposed *benefits*) of nanomaterials are equally as speculative, and perhaps more irresponsible. The paper posed the question in straight-forward terms: 'are nanomaterials hazardous?' Such a question was at the heart of the controversy. Colvin's critics argued first that asking this question was inherently dangerous to the funding prospects of nanotechnology because of the unpredictability of the public and the media. More pointedly, they argued that it was not the responsibility of scientists in nanotechnology, but the responsibility of regulatory agencies and corporations who should test materials before commercializing them. At the heart of the debate was the question of the novelty of nanotechnology, and therefore the novelty of the risks of nanotechnology. If nanotechnology is really new, Colvin frequently argued, then we need really new data about toxicity and exposure, which would require basic science in this area. If however, existing science and toxicology (and regulation) regarding bulk materials is good enough, then it suggests there is nothing genuinely new about the nanomaterials being produced. Furthermore, it raised the question of whether new *venues* were needed—are existing regulatory agencies equipped to deal with nano as if it were not new, or will new regulations, even new agencies, be necessary?

Colvin argued that not asking these questions was as irresponsible and dangerous to humans and the environment as asking them was to nanotechnology's future. Her critics consisted mainly of her colleagues in nanotechnology, chemistry and physics, and the leadership at NSF, including her own program manager. Siding with her in different ways were social scientists, civil society and environmental groups, corporations, environmental scientists and toxicologists.

A key reason for the intensified affect of the debate was the absence of data to argue about. As Colvin puts it: 'We had no data, and we were beginning to speculate... which makes scientists pretty angry.(Vicki Colvin, Interview #1; hereafter VC#1).' In the period between 2001 and 2003, almost no research on the toxicity or exposure of nanomaterials was funded (or conducted) through the National Nanotechnology Initiative (NNI). According to Dunphy-Guzman et al. [7], the NNI spent only 0.5% of its budget between 2000 and 2004 on 'implications of engineered nanoparticles'—the vast majority of which went to CBEN through the National Science Foundation. There were related developments in research, perhaps most specifically in the toxicology of 'ultrafine particles' which were primarily incidentally (not deliberately) produced, and frequently divided into 'naturally occurring' nanoparticles (e.g. produced by forest fires or volcanos), unintentional anthropogenic (such as diesel exhaust, metal fumes or cooking fumes) and intentional anthropogenic (buckyballs, nanotubes, rods and wires) [32].

The lack of data created the possibility for speculation—both about the hazard and about the safety of nanomaterials. With little new research funding forthcoming, Colvin realized (in late 2003) that she needed to change her own research to address the problems she was discussing in public:

> The other thing that happened in 2003 is that I'd had a lot of interactions with EPA and they issued a call. They took all of their nano money [about $16.5 million] and they put it in implications and we basically wrote that call. I did. I went out, I wrote it.... All of a sudden 5 million bucks a year started to flow into the area that wasn't just us [CBEN] and so, somewhere around 2004, I actually switched my research because I realized if I'm out here talking about it, I need to be doing it. So I started to actually collaborate in this project more with the bio-engineers and some of the folks over at environmental engineering. And so 2004 and 2005 was a little bit of a sea change. We started to get data, data that my students were engaged in. [VC#1]

It is somewhat of an irony that Colvin, of the three principals of CBEN, turned out to be the one who would change her research so dramatically in the direction of toxicology, and not the environmental engineer Mark Wiesner (who had extensive experience with the EPA) nor the Bio-engineer Jennifer West. Colvin's desire to change her research seemed to issue in part from the fact that there was no data, but also in part from her reaction to people telling her *not* to do such research. Like many scientists, Colvin characterizes herself as someone who reacts very strongly when people tell her not to do something, or that something cannot be done. Colvin saw this as an opportunity to open up a new direction for research in her lab.

Wiesner, for his part, had also embarked on toxicology research, but opted for a slower and more deliberate entry into the field than Colvin. Wiesner recalls:

> In fact, we started work in that area around the same time but took a very different, and much slower approach from that of Vicki. Toxicology is a landmine of a field and I made the decision early on that it was not the sort of thing you learn to do in between snacks. So rather than try and do the tox work ourselves, we began collaborations with bonafide toxicologists-initially in France (Marseille Medical School), since I had contacts there, and later at UCLA. Ultimately having access to environmental toxicologists and a medical school where we could do that kind of work was a key factor in my decision to come to Duke (Personal communication, 2008).

Wiesner's characterization captures the institutional and disciplinary locations of the different sciences. As an environmental engineer, rather than a materials chemist, his position vis-a-vis toxicology emphasized different aspects, both in terms of its internal complexity and in terms of what he might gain from such a collaboration. Colvin, by contrast, eagerly wanted *data* with which she might argue with her colleagues in nanotechnology and materials chemistry, and not to move into the field of toxicology completely.

CBEN's initial organization provided limited funding for toxicology, and did not refer to it as such. CBEN was not organized around the existing disciplinary lines of toxicology, eco-toxicology, or health research. Indeed, one of the reasons that Colvin's critics within the NSF had given for trying to silence her had been that the NSF does not fund toxicology. Toxicology, they claimed, is more properly the province of the regulatory agencies such as the Food and Drug Administration (FDA), Environmental Protection Agency(EPA), or the National institutes of Health (NIH) and implied that it was not basic science, and definitely not nanotechnology. However, the meaning of 'implications' and the core research science differed depending on the discipline, a fact that became evident in the creation of CBEN. For the environmental engineer Mark Wiesner, eco-toxicology is basic science, whereas for bioengineer Jennifer West, biological toxicology came further downstream, primarily at the FDA, and after the materials had been created. Colvin and her supporters had begun to realize, however, that neither the FDA nor the EPA had planned to treat nanotechnology as special in a regulatory sense, and instead to apply the same tests and standards it does to bulk materials.

Wiesner and West therefore represented two sides of a line that Colvin was trying to walk: on the one hand, a mode privileging *concern* with strong roots in the environmental movement, suspicion of unregulated production, and a way of arguing in which indication of harm is a call to action and control; on the other hand, a mode privileging *control* with strong roots in engineering, a suspicion of government regulation, a belief in unconstrained basic research and a way of arguing in which indication of benefit comes before testing and verification of safety. Colvin's biography places her firmly in the latter camp: a 'born and bred' nano person, specifically materials chemistry and optics of materials and a student of Paul Alivasatos with a widely cited paper and patent on Cadmium Selenide LEDs [5]. But with the founding of CBEN and the interaction with Wiesner and other environmental scientists, with the intense scrutiny of nanotechnology, she has found herself in the former mode as well. Changing her research, therefore, did not imply that she was giving up the mode of control in favor of a mode of concern. Instead it meant trying to find venues in which to synthesize the two modes.

The biggest barrier to this new research direction was that Colvin had no graduate training in biology (much less toxicology or environmental science). Learning the tools and techniques of biology and environmental science posed a barrier to research, rather than a starting point. But in classic form, putting two of her students on projects related to toxicology was a way to learn fast; and a way to work on making her career as well. All of a sudden, a whole new series of experimental tools and systems presented themselves: cell cultures and bacteria, rats and bass, systems biology, environmental science and ultrafine particle toxicology.

The field of toxicology of ultrafine particles was one of the first to present itself as a likely venue for the kinds of questions that Colvin sought to answer. In particular a family trio of researchers: Gunter, Jan and Eva Oberdoerster. Gunter Oberdoerster was one of the leaders in the study of mammalian toxicity of ultrafine particles, and Colvin invited him to present his work to CBEN, with an eye to collaborating on studying the environmental toxicity of nanotechology. Oberdoerster declined and instead suggested his daughter, Eva, whose work was in the area of endocrine disruptors and environmental toxicology, and who ran a lab at Southern Methodist in Dallas. The story of Colvin's collaboration with Oberdoerster, and its breakdown, reveal many aspects of how values in science work themselves into the heart of laboratory research. Colvin's attempt to synthesize the two meanings of implications ramified into a personal story with both predictable and unpredictable elements.

Colvin assigned her student, Christie Sayes, to the project. She sent her to Dallas to learn from Oberdoerster how to do toxicological studies both in cell culture and large mouth bass, of which Oberdoerster had a school remaining in the lab from previous EPA-funded work. For one of the first experiments on the large-mouth bass, Colvin provided the fullerenes from 'the punch bowl'—fullerenes that had been made in-house and solubilized in water at Rice. Sayes lugged a large amount (about 5 litres) of pure fullerenes in water to Dallas which were added to the water in which the fish swam. They conducted standard tests (48 and 96 h exposures) and measured damage to the gills and brains of the fish. They compiled the results and continued with more studies to verify what they were finding: that there was indeed some evidence of damage to the gills and brains of the fish. But it was at this point that the external conditions of the state of nanotechnology research and the dual meaning of 'implications' began to impinge on their laboratory research. Oberdoerster described the first hiccough this way:

> I was running out of fullerenes, so I asked Vicki if she could send some more and she said, 'Absolutely not. I don't like the direction this is going; that you are actually finding effects.' She said 'Honestly I didn't think you would find any toxicity and I don't want this getting out.' And I said oh, ok, that's oh, I see... but' we've done this and a priori we had planned out what we were gonna do and when we were going to publish... (EO Interview #1, 2008, hereafter EO#1)

Oberdoerster felt the situation was especially unfortunate for Sayes. She was in her lab, staying with her at her home and now caught in the middle of what was developing into a professional dispute. Not knowing what to do with this new information, she awkwardly continued the research with Sayes and went back and forth with Colvin through the winter of 2004. She argued that the data was solid, that it was an interesting result, that they were seeing damage but also seeing healing in the gills, and most important that she was eager to get the result out so that others could try to replicate it. Sensing that Vicki did not want the paper published, for whatever reason, Oberdoerster eventually decided to go ahead with publishing the results.

> Vicki, as she realized that this was going forward and getting ready for publication, asked that her name be withdrawn from it, and what she told me was that she never expected there to be toxicity, her whole career is based on these particles, and they cannot be found toxic, because then she cannot go forward with her research. (EO #1)

Colvin also described asking for her name to be removed, but suggested that her reasoning was different. Colvin argued that there was not enough data to be convincing, that the study was set to be controversial, and most importantly, that it dealt only with pure 'underivatized' (uncoated) buckyballs—a form that were not generally commercially available. Taken together these elements enhanced Colvin's sense that the risk to human health represented by these tentative results was probably a good deal smaller than the risk to nanotechnology represented by their publication. Oberdoerster agrees that whatever the reason for Colvin's decision to remove her name, there was tremendous resistance to this line of work, strong personalities in nanotechnology and other factors contributing to the decisions that each of them made about the timing of submission or publication. Add to this, there was a clear sense of the advantage in career advancement that this kind of research represented to both of them; whoever managed to publish first in this new field would be the one who gained the most attention in the media, amongst peers and hopefully with funders.

But there are other confusing and some downright weird aspects to this part of the story. In the winter of 2004, Colvin had already begun her own series of studies on fullerenes and their effect on tissue culture (work also done primarily by Christie Sayes), in the hopes of generating further data that might either challenge, supplement, or perhaps preempt the results that Oberdoerster was getting. Both women started to submit the results of this work around the same time, in early spring of 2004 and according to Colvin, Oberdoerster submitted to *Science* 'right around the same time we tried to submit, which was part of the issue for one of the reviewers because he [sic] clearly had looked at both papers (VC#2).' In addition to claims about the data and its reliability, concern about the style of the research, and the possible risks to the health of nanotechnology by the publication of such work, issues of career advancement and gender also began to play a role. Seen solely from the published literature it seems that Oberdoerster published her study in *Environmental Health Perspectives* in April of 2004 [31], and Colvin published her first study later in *Nano Letters* in August of 2004 [36]. Behind the scenes—or between them—the story is weirder.

Both had submitted to *Science* but neither paper was accepted. The *New York Times* nonetheless tracked Oberdoerster's experiment and publication, and in late March (along with the appearance of her article) ran a profile of Oberdoerster and her study.[11] For Colvin this was not simply a competitive blow

[11] Barnaby Feder, 'Health Concerns in Nanotechnology,' *New York Times* March 29th, 2004

(Oberdoerster both published first, and was profiled in the *New York Times*), but it also revealed and exacerbated a strange set of gender dynamics as well:

> The New York Times did a huge article [with a] picture of Eva... and Eva unfortunately kind of looks like me and so people got me and Eva confused. They would think I was Eva… and this, this is weird, but if you're a woman in science... So there was a TV interview right after that [NYT article] and I was very public in this TV interview, so then the, this connection between me and this New York Times article became very large, even though I intentionally did not take part in [Eva's study], I did not quote it, I didn't want to have anything to do with it, predominantly because... I was trying to walk this very fine line. So, so I became ambivalent myself about taking a public role because the perceived costs, you know losing the center, for example, as a director. (VC#2)

Eva Oberdoerster and fish. From the New York Times, March 29th, 2004

The confusion of Colvin and Oberdoerster, especially by fellow scientists was problematic for more than the obvious reasons of gender inequity and power relations. Oberdoerster is neither a nanotechnologist nor a chemist, but a toxicologist, and her study made a direct leap towards the effect of buckyballs on the whole animal (brain and gill damage in largemouth bass). Even if Colvin were in principle in support of such research, she did not want to be associated with this particular style—or have it confused with what CBEN was created to do, which was primarily to study *applications* of nano to biology and the environment. Colvin claims she had 'scrubbed any recognition of my name or [my grad student's] name from that paper, but I had to acknowledge CBEN because we spent money on the project.(VC#2)'

The 'fine line ' that Colvin was walking implied a difference between the scientific approach to understanding nanomaterials as such, and the 'downstream,' less prestigious and 'risky' (to nanotechnology) toxicology work. As Colvin puts it, most scientists perceive toxicology as a simple question: 'did the rat die?' and not something worthy of funding at a basic level, at a center like CBEN: 'there is something more fundamental here [and] I don't know that I've been able to make that case strongly with my community [materials scientists and nanotechnologists] yet (VC#2).'

Oberdoerster, by contrast, saw little to nothing new in 'nano' toxicology. Given that her father had worked on ultrafine particles since the 70s, that toxicology has a long history of theorizing risk rigorously through defining hazard and exposure, and the fact that synthetic chemists in the pharmaceutical industry routinely asked questions about how to measure and understand the safety of the compounds they created, Colvin's questions seemed like business as usual—or worse, as withholding research findings. For Oberdoerster, it was the perceived threat to a nascent nanotechnology that overwhelmed Colvin's ability to reason clearly about the science. Oberdoerster characterizes the field as full of 'strong personalities' who can get things done but also create problems and pressures that can obscure the science. For Oberdoerster, the work was routine; novel only on the surface because of the material and because of the attention it garnered her by virtue of the media hype surrounding nano.

Colvin's own ongoing study, therefore, tried to walk a 'fine line' by being both a toxicology study and an attempt to explore 'something more fundamental.' Colvin's resistance to participating in Oberdoerster's study was driven by an intuition that new modes of analyzing these materials were necessary—that it wasn't simply a toxicology question about a new material. Furthermore, she knew that 'her community' simply wouldn't care about this research if that were the case. In other words, it had to be formulated in terms which they could experience as within an established 'mode of veridiction.'

Mark Wiesner's comment that toxicology is 'not the sort of thing you learn to do in between snacks' reflects his own concern with CBEN's (and Colvin's) perhaps brazen entry into this already well-established field. Colvin's attempt to forge a form of scientific work that brought materials chemistry to bear on problems for which toxicologists and environmental scientists already possessed tools and a history created exactly the kind of dangerous 'interdisciplinary' middle ground often decried as being neither one nor the other. Wiesner's more diplomatic approach was focused on bringing these fields together around existing tools and practices, rather than trying to forge a new space entirely.

Nonetheless, it's possible to see, even from the published literature alone, how Colvin was attempting to change the nature of the question confronting both sides—to in effect invent a new mode of veridiction. Instead of asking 'is C_{60} toxic?' as Oberdoerster had, Colvin started to ask instead: 'which *species* is most toxic and why?' Given Colvin's background in chemistry and nanotechnology, her concern about the materials in question extended beyond the simple definition of C_{60} as a soccer-ball shaped particle with 60 carbon atoms. Pure buckyballs are obviously interesting—Smalley, Kroto and Curl received a Nobel prize for characterizing them—but practically speaking they aren't particularly useful until they are 'derivatized' or coated in order to increase their solubility, or turn them into substrates to which we can add other molecules for novel purposes. This means that the identity of 'carbon fullerenes' actually includes a huge family of different engineered 'functionalizations.' It is this feature of the control of materials that gives nanotechnology some of its novelty—something that has its closest parallel in the work of synthetic chemists in the pharmaceutical industry, where approaches such as combinatorial chemistry can create a huge array of variations on a single molecule. Each of these different functionalizations might therefore have different hazard and exposure profiles. The prospect of needing to find funding and scientists to study each and every one seemed both impossible to Colvin, and scientifically inelegant. The first paper to be published from Colvin's new experiments, also written with Christie Sayes, appeared in *Nano Letters* in August of 2004: 'The Differential Cytotoxicity of Water-Soluble Fullerenes,' [36], and as the title suggests, focuses on comparing different toxicities of water-soluble species of C_{60}.

The 2004 *Nano Letters* paper is a case study in walking 'fine lines.' The abstract begins by stating 'we show that the cytotoxicity of water-soluble fullerenes is a sensitive function of surface derivatization' suggesting that the question of toxicity is not a simple one, and furthermore, a 'sensitive' one requiring careful scientific experiment and theorization. The article ends, 'this work demonstrates both *a strategy for enhancing the toxicity of fullerenes* for certain applications such as cancer therapeutics or bactericides, as well as a remediation for the possible unwanted biological effects of pristine fullerenes' (emphasis added). Within the abstract—arguably the most tightly and strategically written aspect of most scientific papers—the battle lines over this kind of research are clear: Colvin wants to associate herself with the ability to create new biological applications of nanomaterials, but also to *characterize* their toxicity as a function of their structure. On the one hand buckyballs are toxic, but on the other hand this can be a *good* thing. On the one hand fully derivatized buckyballs are safe (or safer), and on the other hand 'pristine' buckyballs can have 'possible unwanted biological effects.' The article hews to the line that what makes nanotechnology new is the exploitation of the properties that materials have at the nanoscale; what makes Colvin's contribution new is that one of these properties is their *toxicity*—and no one has yet characterized this clearly to her mind.

Compared to the Oberdoerster piece, which remains resolutely in a mode of pure concern—concern over spillage and dumping, accumulation and oxidative stress on cell membranes—the *Nano Letters* piece uses an idiom that mixes concern *and* control calculated to navigate between the two kinds of implications: risks to environment and biology, and risks to nanotechnology. It creates a new 'mode of veridiction'—a new set of criteria for truth claims about nanomaterials. Rather than making claims about toxicity in a language of hazard, exposure and risk, it makes claims about toxicity in a language of engineering and control of matter. Rather than relying on data that would, in a roundabout way, provide evidence for or against actions taken (e.g. by governments or corporations) with respect to C_{60}, Colvin's article presents data that might, in a roundabout way, serve as the basis for engineering materials differently. This new veridiction, however, would only function with an attendant jurisdiction within which it makes sense to make such claims, and this is what Colvin's 'fine line' indicates—the problem of the legitimacy of this new approach.

The last paragraph of the article recapitulates this fine line. On one side: 'This provides striking evidence that water soluble functional groups on the surface of a fullerene molecule dramatically decrease the toxicity of pristine C_{60} (1886).' Which is to say, toxicity exists, but it is an *interesting* problem for materials chemists and nanotechnologists—one related to the properties of the material, its derivatizations, and its surface chemistry. On the other side, a rhetorically complex assertion: 'this work demonstrates that hydroxylation of the C_{60} cage could be used as a remediation for the possible unintentional biological effects of pristine fullerenes (1886).' Coating buckyballs *remediates* possible unintentional effects of buckyballs; which is to say, if they are coated, the possibility that pristine buckyballs have for causing unintended biological damage is remediated—or presumably, prevented to begin with.

Colvin's article does not directly contest or engage Oberdoerster's work, though it does cite it. Many issues are collapsed in the appearance of these two articles—they emerge from different trajectories, represent different ways of making truth claims about materials, different practical approaches to laboratory experiment, and different concerns about the significance of the results. The results of Colvin's study are viewed with skepticism, even hostility, by many toxicologists and environmental scientists, but as Colvin repeatedly pointed out in our interviews, prior to this point [3] there was nothing to argue about—no data and no results concerning new nanomaterials. Skepticism and hostility, however uncomfortable, are much preferred to unwarranted speculation. By 2006, the number of papers had ballooned into a healthy debate conducted over a startlingly large number of journals [33].

Exit Risk, Enter 'Safety by Design'

After these first publications in 2004, research in the toxicity of buckyballs was underway, as were competing definitions of what would count as valid scientific research in this area. During this year, Oberdoerster, together with Mark Wiesner and his students (and with Kristen Kulinowski and Colvin's help) subsequently discovered that the supposedly pure C_{60} that Colvin had contributed was actually not quite pure. It formed aggregates in solution, so-called nC_{60}, which in itself might suggest different effects to be tested for, but more importantly, the solubilization process combined with the formation of clusters meant that some of the toxic solvent (tetrahydrofuran or THF) used to make C_{60} enter into solution remained trapped inside 'eggs' of C_{60}.[12] For Oberdoerster this contamination was unfortunate, perhaps confounding the evidence of damage in her 2004 study, but more than that it represented an unrealistic environmental scenario: C_{60} would never enter solution in lakes and streams and sewers with the help of THF. To rectify this irrealism, she tried adding C_{60} to water and simply stirring it for days until it entered solution, which it slowly did. When some Danish colleagues complained that they couldn't get the same result, she also discovered that it the action of UV light from the window above the stir-plate that helped the solubilization along. Both the action of stirring (wave action) and the presence of UV represented more realistic proxies of an environmental exposure route for the fullerenes.

For Oberdoerster, defining hazard and exposure, and doing so realistically were the priorities. For Colvin, by contrast, hazard and exposure 'realism' was secondary to the characterization of 'differential cytotoxicity'—a result that could be either good or bad, depending on a use case, and might be a route to 'something more fundamental.' To say 'bucky balls are toxic, but this might be a good thing,' as Colvin's paper had, was to emphasize a different problem concerning nanomaterials than that highlighted by the realism of Oberdoerster's approach, in which the toxicity of the substance is implicitly related to its entry into and persistence in the environment in particular 'natural' ways. At the heart of the emerging debate, therefore, was not only a question of whether fullerenes were toxic, but which kinds, how to study them, and in what tradition of research—and at the limit, a definition of what counts as natural and what as designed.

Looking at these first publications in detail, it is thus possible to see the battle being waged *outside* the laboratory. The questions Colvin, Wiesner and Oberdoerster were asking were not bubbling up from laboratory exploration, but channeled into those labs by external debates. The scientific papers could be read on their own as mere statements of fact, as they are rhetorically constructed to do—but when one

[12] The effect of the solubilization process was studied subsequently by Mark Wiesner and colleagues in France, and the results published as Brant et al. [2].

reads more carefully the situation and history giving rise to the papers it becomes easy to see the complex political, and sometimes personal negotiation taking place.[13] In the details of the experimental design and the careful justification of the results, one can chart the course between the 'pure' need for research into the environmental and biological effects of nanomaterials (a rhetorical necessity), and the intense affect, career maneuvering, political struggle and sometimes personal attacks on and among Colvin, Wiesner, Oberdoerster as posing risks to the health of nanotechnology.

The complex negotiation within the science, in the university, and in the public grew out of the confusion around the meaning of implications—risks to biology and environment or risks to nanotechnology? It was only by working through these differences that Colvin and others could start to ask more precise questions in the laboratory—questions different from those asked by toxicologists on the one hand, or nanotechnologists on the other. 'The Differential Cytotoxicity of Water-Soluble Fullerenes' is neither normal science nor paradigm-shattering, but a kind of strategic working over of the demand for responsibility, into a form of science that is both application and implication at once, both concern and control*: it was an attempt to define safety as a fundamental property of materials.*

For the first four years of their work in CBEN, Colvin and executive director Kulinowski had pitched the story of 'Wow to Yuck?' asking whether the initial love-affair with the benefits of nanotechnology would turn to a repugnance when facts about their danger to biology and environment emerged. Such a framing was useful because it integrated the two kinds of implications—though not intentionally. If heard from the perspective of nanotechnologists, the story was all about public perception of nano and risks to its health, if heard from perspective of toxicologists or social movement activists, the story was about the need to study hazards and risks of new materials. Neither message was quite what Colvin aimed for. But then, a revelation, a moment on the road to Damascus (or in this case, perhaps it was D.C.), when Colvin discovered a different way to integrate these two risks:

> I was on the road promoting it [the new research] and then a bizarre thing happened. It was really quick but all of a sudden I hit upon a message of how to pitch it—and this this would not have happened if I wasn't doing it—and this is what I do take credit for. So I was struggling with Rick [Smalley] hating what we did—he still hated what we did. And a lot of my own community—I'm a nanotechnologist right—so my own community was, I was becoming kind of... I mean it was, it was pointed, things I was not invited to, places I had been before, you know. My thesis advisor taking me aside and saying 'do you realize what you're doing?' You have to realize it's always couched in the science and the quality of the science and I kept saying 'it's an early area. How can you be doing science yet? It's just starting.' But I hit upon a way to do it and that is the 'safety by design' idea, the idea that you can study implications and from that go back and engineer materials and processes to be safer and to have less of the impact that you don't want them to have... Once I flipped it, labeled it 'safety by design' and started to push it, I stopped using 'wow to yuck?' cause I got all kinds of crap for that. (VC #1)

'Safety by Design' appealed immediately to chemists and nanotechnologists, without giving up on the fundamental message of risks to human and environmental health. It was a very clever label for the research CBEN saw as its core mission—both safety and engineering. But as with any such label, it brought with it a whole new set of challenges. Toxicologists, according to Colvin objected: 'It turned out, it pissed off a lot of the toxicologists, because they were, like, 'well how do you *know* it's safe?' It was a very good question. Toxicologists raised a concern over conflict of interest: if the goal is to engineer safe materials, then of course the engineers *qua toxicologists* are going to find that it's safe. Colvin's somewhat flip response to this was that the same accusations might be leveled at toxicologists: if they demonstrate toxicity, their funding remains safe. But it nonetheless remains a good question: what is the meaning of safety? How is it defined and by whom? What would meaningful agreement on safety look like? 'Safety by design' angered the toxicologists because it presumed that

[13] This claim is related to recent work by Melinda Fagin which makes a strong case for assessing justification by looking beyond the papers into the social context generating them [9].

safety was an issue of design, not a feature of the established risk framework of hazard levels and exposure routes; on the other hand chemists and nanotechnologists were more comfortable with the message:

> It made my community feel better, because [having the data] taught... them where the chemistry is. They got to see the science. They understood oh yeah, biological properties, they're interesting, they can be general [laughs]. They're not just 'did the rat die?' We can talk about what happened! ... I think the time I knew I had fixed it [was when] NIH had a big unveiling of their nano program and they invited eight academics. Two were from Rice, one was Rick Smalley and one was me; we only had eight minutes, it was a big dog and pony show and it was web cast everywhere and I really pitched the safety by design idea and Rick loved it. He just thought it was great and I got away completely from 'it's bad, it's going to kill us all, I found a way to pitch it that, that he really related to. (VC#1)

Colvin had successfully not only walked, but actually dissolved the fine line. She saw her work as re-positioning the various disciplines involved around the materials they worked on and the kinds of questions they asked. Rather than a classic, modernist hierarchy of science with chemistry as fundamental science and toxicology, biology and environmental science as lower in the hierarchy (or outside it altogether), this new configuration brought biology, environmental science and toxicology into competition with physics—as sciences that provide resources for nanotechnologists to characterize the relationship of structure and function of new materials. Perhaps even more important, it was a message that Colvin could use to make her own career—to become the person identified with the engineering of new materials for the purposes of safety. History may or may not reward her with this recognition, but the goal and the success were real enough as they happened.

CBEN began its life with a vision of 'applications' of nanotechnology to biology and environment—medical diagnostics, cancer cures, environmental remediation with membranes and so forth. With 'safety by design' Colvin managed to re-assert this vision, but with safety as a new key component—a new 'function' around which applications of new materials can be characterized. To say, as they did in their first paper, that buckyballs are toxic, *but this can be a good thing*, was a key feature of this approach. Toxicity and exposure routes are fundamental properties—if we choose to exploit new materials for whatever reason we need to know not only properties like strength and conductivity, but safety and exposure as well—they must be made theoretical, they need a mode of veridiction.

However, 'safety' is not just one application among others—it potentially affects every other field of application as well. It moves the fields of biology, toxicology and environmental science from being resources in terms of a potential field of applications, to resources in terms of a potential field of explanations, constraints and systems for control and regulation. Colvin's bid to make her career in the same way as her advisors and mentors (quantum dots and LEDs for Alivasatos, carbon nanotubes and energy for Smalley) might not be just one success alongside others, but one that could potentially demand a reconfiguration of the kind of science everyone in nanotechnology and materials science pursues. It should come as no surprise that the proposal is met with such intense emotion and affect if it means that it directly affects the style, life and work of a large segment of scientists—not just in nano, but in toxicology and environmental science as well. Similarly, the approach implies that, while toxicology is essential to this reconfiguration, its *theories* of risk and hazard are inadequate to the issues raised by nanomaterials; it suddenly appears insufficient to seek data about the risk and hazard of every new material and every functionalization of every new material. Rather, it creates a new mode of veridiction—a new set of truth claims about safety as a fundamental property of matter, claims that might be made about wide classes of materials and their uses and ultimately replace one version of risk analysis ('is it safe?') with another and quite different version ('how do you engineer towards safety?')

The Wages of Safety

'Safety by Design' opened up a range of difficult questions. Far from being a scientific 'breakthrough' or a simple scientific fact (things many studies in the history and philosophy of science have demonstrated are hard won), safety by design is more like a solvent: it decomposes and reveals. Colvin's work on this idea was born in controversy—both public controversy over a threat to a new field and its funding as well as more conventional scientific controversy over the validity and legitimacy of her methods and findings. As CBEN and ICON continued to pursue the question of implications, and others in the emergent field of nanotoxicology have continued their work, a series of ramifications have followed. Many of these, it is clear, have emerged because of the combination of the new venue of ICON, which in its capacity as a kind of membrane, channeled the ramifications both into the lab and back out again and the attempt to make new kinds of truth claims about safety as a fundamental property of materials. Several of these ramifications are worth noting briefly.

First, safety by design re-opened a question about predictive toxicology—can it be done and how? Toxicologists, especially those in the pharmaceutical industry, have long been asking this question. CBEN and ICON as institutions had no ties to the pharmaceutical industry, but as questions formed about how to assess the potentially huge class of materials emerging from nanotech labs, Colvin and others turned to the field of 'Quantitative Structure-Activity Relationship' modelling (QSAR). QSAR modelling has had modest success in screening compounds for toxic characteristics in the design of new pharmaceutical compounds [17, 18, 22]. It is controversial amongst some biologists however, because of its overly simplistic model of metabolism. For many biologists, and toxicologists like the Oberdoersters, it is clear that molecules are transformed by the environment and transform the environment in turn. Livers, lungs and skin metabolize and change molecules, and things like UV light and simple motion can transform a material in the body or the environment. Colvin counters that nanomaterials are much smaller and simpler (and arguably better understood) than complex bio-molecules, but the question remains an open one.

Second, safety-by-design also raised questions about differing definitions of nature that divide biologists and nanotechnologists. Bensaude-Vincent [1] has detailed the subtle differences between versions of nanotechnology that either engineer biomolecules or take inspiration from them for design. Similarly, Colvin's immediate community of materials chemists and nanotechnologists have a far more engineering-oriented approach to biology,which means that systems biologists and others attempting to understand biological entities in their 'natural state' find their approach of nanotechnolgy to be dirty and uncontrolled. As Colvin puts it: '[systems biologists] kind of feel like, if we don't understand the natural state why would we want a perturbation coming in, right? What will that tell me? They're interested in using quantum dots as tags and fluorescers and all that good stuff but I think to engage the biologists we're going to need another couple of years to come up with some good mechanisms for interactions. (VC#1)' For many in nanotechnology (in a way similar to the field of synthetic biology), nanomaterials are probes for exploring what happens in different contexts, under the assumption that it will tell us something about structure and function.

Third, related to this is the issue of what standard contexts will define the meaning of 'biological' or 'environmental' in this new domain of safety by design. Ongoing experiments use fish, rats, human cells and other proxies for the human body and its safety. These choices have effects on the validity of claims made in this new venue—are we all using the 'same' human cells, and do we (nanotechnologists) know how to handle them? A mode of veridiction in which Colvin and others might claim to have engineered a 'safe' material also requires a mode of jurisdiction in which standardized tools, standardized nomenclature and standardized organisms allow these new claims to stick. If it is only Colvin's lab that tests buckyballs in human HeLa cells, then the claims made thereby will have no juridical force amongst other researchers—beyond unverifiable, they will simply have no legitimacy to other researchers. If CBEN and ICON are successful in establishing new venues for this kind of research however, it establishes the beginning of a jurisdiction based in the standardization of media, tools and organisms for a small and growing community.

Finally, safety by design has also raised a new challenge to the definition of materials and their environmental regulation. In part because of work within ICON to identify 'hot spots' in the life cycle of materials (a methodology introduced into discussions at ICON by Mike Garner of Intel), research in this area has focused on workplace manufacture and handling of these materials. In subsequent work with Georgia Tech colleague Joseph Hughes [11], the implications of Colvin and Wiesner's work on nC_{60} are connected more explicitly to the domains of regulation and workplace/industrial handling of nanomaterials. Specifically, the article demonstrates how 'in aqueous systems, nano-C_{60} behaves neither as an individual molecule nor as a bulk solid (4315). From this they draw conclusions that standard measures of the prediction of toxicity (e.g. for 'polyaromatic hydrocarbons') are inadequate: 'this work clearly illustrates the limitations of the current guidelines for the handling and disposal of C_{60}, which are based entirely on the properties of bulk carbon black...these guidelines may need to be revisited. (4315)' Worker safety, as a 'hot spot' in the life cycle of nanomaterials therefore enters explicitly into the kinds of questions asked in nanotoxicology.

Conclusion

By mid 2008, the question of whether safety by design would succeed as a new mode of verdiction remained open. CBEN and ICON were actively looking for ways to continue their work (CBEN's funding ends officially in 2011) and to take the idea into new areas such as water treatment with magnetite nanocrystals and an attempt to innovate a form of 'open-source nanotechnology' [27]. In reflecting on its success, Colvin makes a strong case that even the limited amount of research so far conducted has changed the way chemists think about their materials:

> What's happening now is really an interesting process of, of separation because now this issue [toxicity and hazard] is being used by nanotechnologists to differentiate their materials from somebody else's. "Use gold because it's totally safe, don't use quantum dots, they're going to kill you," you know. So now what I get from my own technical community is in large part determined by what they make and what, what particular thing they're into. (VC#1)

The fact that nanotechnologists research and careers are closely tied to expertise with a specific material means that making 'safety' into a fundamental property applies to everyone working with nanomaterials: quantum dots, rods, buckyballs and nanotubes and so on. Different 'communities' of researchers formed around these different materials are handling such information differently, and as Colvin and other researchers continue to conduct research on different materials. This ongoing research includes an article on the toxicity of functionalized Carbon nanotubes [38, 39], one on the toxicity of nC_{60} [37] and two on the toxicology of titanium dioxide [38, 41], each of which has drawn more and more nano-scientists into the debate.

> Now we're in the secondary backlash [that] is more pointed, poignant, in that now that the data is emerging there are particular materials and particular issues about certain classes of materials which are very significant or potentially significant and those communities are then pushing back... So quantum dots for example: you can't get a Q-dot bio-imaging proposal through NIH right now because of the toxicity of quantum dots; and that community is handling it well. That community is owning up to it saying, 'Well, duh! we've got cadmium in there you know, we're not idiots. We've got to figure out a way to deal with this and we're going to make alternative quantum dots and we're going to learn how to wrap em up real tight and...' So I think that community is rolling with it. The carbon nanotube and carbon nanostructure community on the other hand is not. They are much more reactive...(VC#2)

The differentiation of researchers based on the toxicity of their materials is new (to the chemists); never before has it been their task to manage and understand this aspect of their materials at the stage of characterizing them for a particular function. By the same token, very little information exists to date, so the anecdotal claim that the NIH is resisting proposals for quantum dot bio-imaging might suggest that it has taken a more precautionary stance than ever before; a stance in which it expects researchers to find ways to 'wrap 'em up real tight' in a manner that is convincing to their peers and not only to the 'downstream' regulators such as the FDA, EPA or toxicology communities. This shift in the configuration of power, in which nano-scientists are now paying more attention to such issues is by no means simply about the success of 'responsibility' or 'ethics' but also has to do with the active work of creating a novel field in which *new* things can be produced—new 'structure-function' relationships that are both useful in terms of safety (mode of concern) and useful in more conventional terms of understanding how to control matter (mode of control).

Thus, the evidence that buckyballs might be toxic, but this might be a good thing. Understanding such a claim means getting over the language of applications and implications, on both sides of that debate. Simplistic assertions of good and evil (buckyballs are toxic, watch out!), or absolute statements about precaution and danger, or risk and responsibility do not capture either the development of the science or the response and reformulation of ethics at work. Getting over implications and applications (going beyond good and evil), however, does not mean going beyond good and bad, but attending to the rank ordering of values taking place in the changing configuration of nanoscale science and engineering. There is an ongoing struggle within science to redefine how values will be incorporated into scientific research—and this is also something that drives the research itself. The different modes of veridiction represented by toxicology and materials chemistry are synthesized into a new one by the invention of safety by design. Furthermore, such a mode is not just a result of one scientists' new claims, but requires the invention of new venues within which one can conduct such research, the definition of new modes of jurisdiction that can adjudicate (across materials chemistry and nano-toxicology) standards by which truth claims are judged and ultimately the creation of new objects, like functionalized buckyballs, which literalize these new configurations of knowledge around a usable, and very real, object.

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Interviews

VC#1: Vicki Colvin, Interview #1, May 2007
VC#2: Vicki Colvin, Interview #2, July 2007
EO#1: Eva Oberdoerster Interview #1, April 2008