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**ETHICS IN BIOLOGY,
ENGINEERING, & MEDICINE
AN INTERNATIONAL JOURNAL**

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Brooklyn, New York 11203



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With contributions from leading clinicians, ethicists, industry leaders, philosophers, researchers and scientists, we aim to provide a forum for improved understanding of the ethical challenges that face us with the rapid progress of biomedical sciences, biomedical engineering and clinical medicine. *Ethics in Biology, Engineering and Medicine* (EBEM) publishes original articles, reviews, brief reports, case studies, commentaries, book reviews and correspondence. Occasionally special issues will be published addressing specific interest topics (e.g., clinical trials, animal research and nanobiotechnology).

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Nanotechnology in Biology: Understanding Future Ethical Dilemmas from Past Technologies

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ABSTRACT: There is a growing debate about ethics in nanotechnology, the control and manipulation of matter at a near-atomic scale, in which particles have the potential to redefine the rules of physics, chemistry, and biology, opening the door for astounding technological advances. The issues that comprise this evolving debate surrounding the intersection of ethics and nanotechnology are challenging and complex. Scientists with opposing opinions and different agendas have been defending their views since the advent of nanotechnology, especially as nanotechnology research begins to shift from electronics and information technology to biological and medical applications, or “nanobiotechnology.” Skepticism and fear flow from futuristic predictions of nanobiotechnology applications in the same way that hope and excitement do from research currently happening in the field. While it is nearly impossible to anticipate all of the ethical issues that will arise from the application of nanotechnology in the life sciences, some dilemmas are so commonplace for emerging technology that we can reasonably predict that there will be similar issues raised by nanobiotechnology. This paper discusses ethical issues anticipated from the emerging field of nanobiotechnology for applications that are not futuristic, but are on horizon in the 21st century, while looking at case examples and lessons learned from emerging technologies in the past.

KEY WORDS: nanotechnology; ethics; biotechnology; nanobiotechnology; nanoethics; biology; medicine

I. INTRODUCTION

A. Nanotechnology and Biology

The US National Nanotechnology Initiative (NNI) defines nanotechnology as the understanding and control of matter at dimensions of 1 to 100 nanometers, where unique physical, chemical, and biological properties emerge.¹ Nanobiotechnology is defined as an extensive field of knowledge that applies nanoscale principles and techniques to understand and transform biosystems; it uses biological principles and materials to create new devices and systems integrated at the nanoscale.² The promise of new technologies to improve health and human life appear to be endless with nanobiotechnology.³ New analytic and diagnostic techniques are aiding researchers in understanding molecular actions that provide new insight into different biological pathways. These techniques can improve current methods for the screening, diagnosis, and treatment of disease.

New techniques in molecular medicine are transforming the biopharmaceutical industry for targeted drug delivery and advanced therapeutics based on the information obtained from the human genome. Sensors are under development for disease detection and management due to the ability to make molecular recognition of biomarkers smaller and more sensitive. With the advancement of nanomaterials that are biocompatible with the human body, nanostructures are being developed for repairing damaged tissues or longer-lasting implants. Finally, nanobiotechnology has great potential to affect the health of the environment in terms of wastewater treatment and remediation, pollution control, and ecological preservation.

The promises and expectations of nanobiotechnology are immense for human and environmental health. However, the field is advancing so rapidly that the dissemination of health and safety information lags behind innovation, leaving society confused, skeptical, and, at times, fearful. Ethical, societal, and legal implications of nanotechnology are generating controversial discussions among all stakeholders. It is unclear whether traditional ethical principles can be applied to this new technology, if standards need to be set on a case by case basis, and who should be in charge of ensuring safe and ethical conduct within the field. While we are able to list a number of current and potential benefits of nanotechnology, the role of ethics comes into play when the potential risks and consequences are unclear.

B. Economics of Nanobiotechnology

Affecting the global economy greatly, nanotechnology has been heralded as ushering in the next industrial revolution.⁴ In the next 5 years, nearly 75% of the innovation research and development of nanotechnology industries is projected to be driven by the health-care sector, and a \$450 billion nanotechnology-enabled medical and biological market is expected.⁵ Other analysts have predicted that by 2014, the market for pharmaceutical applications of nanotechnology will be close to \$18 billion annually.⁶ Other sources show that the United States' demand for medical products incorporating nanotechnology will increase more than 17% per year to \$53 billion in 2011 and \$110 billion in 2016.^{7,8}

Policy framework and funding mechanisms for science and technology typically revolve around priorities identified by the stakeholder groups involved. Since 2005, collective investments from the NNI for research on ethical, legal, and societal implications of nanotechnology have totaled over \$260 million.¹ The NNI invests time and effort into public-private-university collaborations in an effort to address a variety of environmental, health, and safety issues germane to nanotechnology through the lens of ethics in ways that industry is not typically equipped to address. The two largest funders of ethics research are the National Science Foundation (NSF), which focuses on education, and The Defense Advanced Research Projects Agency (DARPA), which focuses on ethical standards and guidelines. The National Institutes of Health (NIH) also currently funds research related to nanomedicine, with a focus on the advancement of safe and effective clinical applications.

C. Ethical Agenda for Nanobiotechnology

The generation of emerging scientists, engineers, industry leaders, and policy makers in the field of nanotechnology and biological sciences will play a critical role in ensuring the vitality, safety, and ethics of the coming nanoeconomy. An informed population of developers, adopters, and users will be responsible for communicating to the general public the nature of nanobiotechnology, its contribution to a strong global economy, and the promise it holds for improving lives. The following elements are crucial components of the ethical agenda for nanobiotechnology:

- Identification of valid health and environmental concerns
- Development of a clear and robust regulatory environment
- Design of ethical guidelines that accompany the development of new technologies affecting society at every level
- Creation of a positive view of the benefits of nanotechnology while ensuring that real dangers in nanotechnology are clearly and reasonably addressed.

Although advocating that a proactive ethical approach be taken among stakeholders seems straightforward, two major issues arise. First, with numerous incongruencies about the implications of nanobiotechnology, each stakeholder group is reluctant to take the lead in creating policies and enforcing regulations within the field. The specific physiochemical parameters (e.g., size, shape, surface characteristics, charge, functional groups, crystal structure, and solubility) that most strongly influence biological activities remain unknown.^{9,10} Scientists do not want to forestall research, regulators are charged with ensuring public safety, and the general public is relatively uninformed with regard to accurate, reliable information about potential benefits and harms associated with nanobiotechnology. This is a prime example of an innovation paradox known as the Collingridge dilemma.¹¹ As a technology advances through the research and development process, decision making will become narrower for industry and regulatory agencies, but at the same time, increasing public interest and awareness of the technological innovation as it nears its final stages could change or delay the innovation process completely.¹² Based on different elements of time, power, and knowledge, this paradigm is worth considering to protect the interests of the general public without delaying the progression of nanobiotechnology.

Second, critical shortages are being predicted in developing a nanotechnology workforce: those who will manufacture, apply, and use nanobiotechnology in health care settings, public health applications, and environmental interventions, as well as researchers.¹³ By infusing nanotechnology education into science, health, and sociology curricula, the next generation will acquire the knowledge to deal with this emerging technology. It is also important to recruit a strong nanobiotechnology workforce for the next decade of needed research and innovative breakthroughs. A diminutive number of

established nanotechnology education programs address issues in ethics, economics, health, and environmental impacts or societal perceptions.¹⁴ Training for this workforce should include real-world ethics training and strong mentorship for the most effective professional development.

In addressing the ethics of nanobiotechnology, it is evident that legal implications, societal perceptions and involvement, and regulatory issues are intertwined. Identified as leading topics for nanobioethics divided by different disciplines and stages of the technology, this paper examines issues pertaining to workers handling and researching nanotechnology applications in biology, medicine, and the environment. By giving case specific examples of technologies from our past, our intention is to describe similarities for the ethical adoption of nanobiotechnology as the field advances.

II. NANOMATERIALS AND MANUFACTURING: AN INDUSTRIAL PERSPECTIVE

A. Occupational Health and Safety: Radiation

Hazard surveillance in industrial settings involves identifying and characterizing potential hazards in the workplace in order to identify toxic agents, work processes, and individual workers at risk of exposure to reduce overall exposure through early intervention.^{15,16} Awareness of these factors also provides insight into the effectiveness of existing engineering controls and personal protective equipment used to prevent illness and injury.¹⁷ The physiologic and health outcomes of occupational exposure to nanomaterials have not yet been characterized or documented, nor have the details surrounding the toxicity of various nanoparticles. Health concerns include inhaled aerosolized nanoparticles (potential pulmonary toxicity) or nanoparticle penetration of skin (dermal translocation and biodistribution to other organs) during the research and manufacturing stages.¹⁵

Currently, there is ample information for numerous organizations to recommend treating engineered nanoparticles “as if” they are hazardous in the workplace. The use of nanomaterials in food, cosmetic products, and medicine changes the players involved in the decision-making and regulatory processes. The federal regulatory structure for nano-industries is fragmented, as the involved agencies have different priorities. For example, the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) have issued inconsistent guidelines on nanomaterials in products and manufacturing.¹⁸ Combining the ethical concerns of biotechnology with nanotechnology generates topics of much debate. To address these issues, it may be beneficial to organize a forum similar to the Asilomar Conference of 1974, where federal experts sponsored a meeting for scientists to discuss the issues and set an agenda for biotechnology ethics.¹⁹ While the assessment of the potential toxicity of nanoparticles is at an early stage, researcher awareness and the development of occupational health and safety programs, including hazard surveillance and risk management, are strongly recommended.²⁰

Public health lessons have been learned when the rapid development and deployment of technology outpaces our knowledge and understanding of issues associated with health and safety.²¹ One example of a biotechnology that holds significant medical

promise for diagnostic and therapeutic applications is radiation and the use of radium. Over the course of more than 100 years, the dangers of interactions between radiation and biological tissue became apparent, but research on the potential harms greatly lagged behind the technology. This serves as a good example for occupational health and safety researchers, because the workforce involved in developing new ways to use radiation and radium are at the greatest risk of injury or death due to exposure to radiation.²² Before proper controls and regulations were put into place for radiation, millions of people were injured or died from the effects it had on their health.

B. Intellectual Property and Legal Issues: The Human Genome

Universities and private research organizations are patenting nanotechnology applications at an increasing rate. A significant barrier that industries investing in nanobiotechnologies are faced with includes freedom to operate and intellectual property issues. Biotechnologies enabled through nanotechnology have become highly visible, resulting in a large number of patent owners, each having some right to exclude others from replicating various aspects of their invention. As a result, for an organization to commercialize their nanotechnology product, it may have to obtain permission from numerous patent owners. How industry and society overcome legal struggles such as these may be dependent on their understanding of the issues relating to equity and fairness, nondiscriminatory license practice, incentive to innovate, and the division and aggregation of legal rights.²³

The completion of The Human Genome Project almost a decade ago has fueled debate about how genetic information is obtained and used. This is a prime example of a breakthrough in biotechnology in which the ethical and legal issues have been thoroughly debated and can be anticipated with regard to emerging nanobiotechnologies. It is also an example of property rights in which patents cover conventional products not considered nanotechnology, protecting the innovation's concept and not limited by scale. Applications using nanoscale technologies have further changed the way genetic information will be accessed. Although still in the research phase, nano-microarrays will make genomic information readily accessible at very low cost to a majority of the population. As the field of genomics and subsequent genetic data increase, new legal issues will continue to evolve for researchers, policy-makers, consumers, and private industry.

Regulating biotechnology applications such as those used to decode the human genome has been difficult for decision makers due to issues of privacy and intellectual property. Regulators should assist industry in creating standards for the ethical development and deployment of such biotechnology applications, as well as how to control the outputs, as in the case of selling genetic information. These companies must be held accountable for disseminating accurate information, including the ability to make an association between a disease and a DNA sequence. For some complex conditions, environmental factors are still considered a determinant, and all of the genes that contribute to risk have not yet been discovered. The ability to control access, protect confidentiality, and ensure accuracy regarding genetic information is necessary to protect the public.

III. NANOMEDICINE

A. Clinical Applications: Newborn Screening Program

Nanobiotechnology applications in medicine and public health will lead to revolutionary advances in the prevention, screening, diagnosis, and treatment of disease. This up-and-coming discipline called “nanomedicine” will require cross-disciplinary research and communication between basic science researchers and clinicians. The NIH describes nanomedicine as the application of nanoscale scientific concepts and engineering principles to medical diagnosis, monitoring, and treatment. As such, nanomedicine involves “highly specific medical interventions at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve.”²⁴ Nanotechnology applications in medicine will lead to revolutionary advances in targeted drug delivery, imaging, diagnostics (e.g., quantum dots), implant technology (e.g., increased biocompatibility), regenerative medicine, anticancer therapies (e.g., magnetic hyperthermia), infectious disease control, and personalized medicine. Practitioners embracing novel applications and concepts in nanomedicine must gain the knowledge needed to incorporate new biotechnologies into clinical practice and enhance their ability to deal with the ethical ramifications. Federal and state funding agencies also need to allocate appropriate funds for health and safety research in nanomedicine, and stakeholders should take a collaborative, proactive approach regarding human health and safety.

Ethical considerations for clinical applications range from realistic concerns of biocompatibility, immunogenicity, toxicity, and stability to futuristic fears such as human enhancement, singularity, and eugenics. One of the most relevant ethical debates is generated by the speed and quantity of diagnostics and screening techniques preceding therapies enabled by nanobiotechnology. “Lab-on-a-chip” technologies are being developed to produce high-rate screening modalities in which many diagnostic tests can be completed simultaneously on one chip. Physicians will have the ability to screen for more diseases, mutations, and genetic alterations at a cheaper and faster rate. It is argued that the burden of knowing about predispositions or a diagnosis with limited treatment options is more detrimental to quality of life for some people. The adoption of these rapid screening tools has the potential to change the way people routinely manage their health information, and may put them under pressure to make difficult decisions regarding the outcomes of such tests.

One example of this issue is newborn screening in the United States. This is a program in which the promises have been realized after implementation: every year, about 3000 infants develop normally instead of being burdened with severe liver disease, physical disability, or mental retardation.²⁵ In this example, ethical dilemmas often stem from the socioeconomic status of individuals in society. A family might have information from the newborn screening program, but struggle in obtaining the appropriate resources to address the diagnosis or face the burden of a disease that currently has no treatment. New nanobiotechnologies have the potential to exacerbate health disparities when these new technologies call for more individualized or costly therapies and

treatments, or when those marked by a specific genotype or disorder can be identified. Advances may also give families information about a potential predisposition that they then have to make a decision about without any further information. Similar issues arise in some cases of cancer screening and early detection. High-throughput screening is changing the way we detect and diagnose disease, but how beneficial is it if we do not have the resources or proven therapies to alleviate the burdens?

B. Public Health Applications: HIV Transmission Studies

Innovations in nanobiotechnology have the ability to aid developing countries with solutions to some of the most troubling threats to their health and existence. For example, medical applications have been used to create less-expensive vaccinations that can be administered in fewer doses for diseases that plague third-world countries. Access to clean water, a major contributor to health outcomes, is diminutive in these countries due to determinant economic factors such as poverty, low educational attainment, and inequality. New clean-water technologies have now been identified, and are expected to be cheaper and more efficient than the traditional water filtration and treatment systems. These are two examples of nanobiotechnologies identified to revolutionize and improve global health. However, as with any new technology, it is necessary to ask, how can countries and populations who need these technologies to improve their health and standard of living overcome barriers related to accessibility, affordability, and fair distribution?

Continuous ethical debates about testing, distribution, and education about different medicines and vaccines in developing countries are exemplified by HIV-transmission studies. Typically, research subjects are selected from vulnerable, uneducated, or underinformed populations. By the late 1990s, there was outrage about studies in which the controls were not receiving the best standard of treatment, clinical outcomes did not benefit subjects in the long-term, and early effects of the drug were unknown or unclear even to researchers. Basic human subject research protection needs to be adequately maintained to ensure appropriate testing and use of new drugs and vaccines.²⁶ Analyzing the distribution of medicines such as azidothymidine and tuberculosis vaccines reveals that education for the populations using them is minimal. Interventions to educate and empower third-world populations in dire need of these medicines, as well as follow-up care to ensure that drugs like these are used properly, are urgently needed.

IV. NANOTECHNOLOGY AND THE ENVIRONMENT

A. Sustainability

Nanobiotechnology offers new tools for the sustainable development of applications in energy as well as ways to improve and maintain failing ecosystems. These applications can be of significant support in meeting the needs and demands of an expanding and increasingly urbanized population and of developing countries that have a poor quality of life due to limited resources. Examples include environmental remediation to clean

up heavy metals and chemicals, pretreatment for fuels to reduce the presence of harmful compounds, waste management and bio-monitoring, and water purification.²⁷ These applications offer promises of greener technologies, a reduction in costs, solutions for climate change, and natural resource conservation.

While nanoparticles are a concern in industrial processes due to waste management and distribution, it is of equal or greater concern how nanoparticles will affect the environment when used directly in these environmental applications. Research funding is directed toward obtaining information on nanomaterials throughout their entire life cycle. Because their properties and functions may change at each stage, from material suppliers, transport, research and development, manufacturing, packaging, and consumer use and disposal, it is crucial that we understand the potential risks throughout the life cycle of the nanomaterial or nano-enabled product.

One familiar example of a technology used for its outstanding properties in science is polychlorinated biphenyls (PCBs). Due to their non-flammability, chemical stability, high boiling point, and electrical insulating properties, PCBs were used in hundreds of industrial and commercial applications, including electrical, heat transfer, and hydraulic equipment; as plasticizers in paints, plastics, and rubber products; in pigments, dyes, and carbonless copy paper; and in many other industrial applications.²⁸ Although PCBs were banned almost three decades ago, they remain in the environment from their manufacture and use in the United States prior to the ban. Researchers have identified that PCBs do not readily break down, and therefore can stay in the environment for long periods of time, cycling between air, water, and soil. PCBs have been found all over the globe because of their ability to transport while cycling through different ecosystems. Their remnants and by-products have been shown to accumulate in the leaves and above-ground parts of plants and food crops, and to bioaccumulate in small organisms and fish, which may then be ingested by humans. Further research has determined that PCB exposure may contribute to the development of some cancers, and may lead to many other adverse effects on the immune system, reproductive system, nervous system, and endocrine system.²⁹ We have incomplete knowledge of how materials and particles used in nanobiotechnology applications enter, interact with, and exist in the environment. More research is needed on each material's risk, as well as on its biopersistence and transport through various ecosystems.

B. Food and Agriculture: Genetically Modified Organisms

In 2006 in the United States, there was a \$15 million investment in projects for "agri-food" applications in nanotechnology.³⁰ Currently, nearly 100 readily available consumer products in the food and beverage industry incorporate or contain nanotechnology.³¹ Current applications include biosensors used to monitor crop growth, pest control, and quality control in food production; nano-membranes used for food processing, nano-emulsions used in agricultural chemicals, methods for more efficient food packaging and preservation methods, additives in diet products claiming to work faster and better, and nano-ingredients used for nutritional purposes. The FDA is the primary federal

agency responsible for ensuring the safety of commercial food and food additives. To date, they have advised producers of food using biotechnology—and now nanotechnology—to abide by the traditional regulations set forth for food distribution. Likewise, food labeling of nano-ingredients is voluntary for each company.

This topic is relevant in the discussion of ethics, because products are already on the market, the public has easy access to them, uncertainty exists with regard to regulation and labeling, and the example of food has been heavily debated from a biotechnology standpoint in regard to genetically modified organisms (GMOs). Many basic controversies have been identified with GMOs: potential human and environmental health impacts, an increased separation between industrialized and developing nations, biopiracy, tampering with nature, misleading information and lack of education for consumers, and regulation. We should consider some of the lessons learned from the case of GMOs for the application of nanobiotechnology in food and agriculture. These include the need for increased transparency in safety assessments and mandatory product labeling, proactive approaches by agrifood industries, and increased public involvement in the decision-making process.

V. DISCUSSION

The emerging field of nanobiotechnology represents the application of specific nanotechnologies to the principles, structures, and substances used in basic life sciences, creating the means to advance research to higher-dimension objects, integrated devices, and systems.³ It is obvious that nanobiotechnology will affect many different aspects of human health, public health, environmental safety, sustainability, and dynamics of society. It is also clear that there are a multitude of stakeholders who are jointly responsible for different aspects of each individual technology. Looking into some of the past examples presented in this paper while considering the unique properties of nanotechnology applied to biological systems, it is recommended that the ethical agenda and oversight of nanobiotechnologies be evaluated on a case-by-case basis and consistently communicated with regulators, researchers, and the general public.

As identified by this review, there are three key actions that need to be continuous throughout the progression of nanobiotechnologies. First, education of the nanotechnology workforce is imperative. This includes current workers in manufacturing, research, and development; students and the next generation of scientists preparing for careers in nanobiotechnology; and workers in diverse fields in which nanotechnology will be introduced over the next several years, such as physicians and pharmacists. Although there are gaps in our understanding of the risks and benefits in the fusion of nanotechnology and biology, curricula and recommendations should be created and continuously updated as new information is gathered.

Second, communication and planning within the ethical agenda should be maintained, organized, and structured for all stakeholders. This requires academia, industry, and government to be proactive about gathering and disseminating data, conversing with the general public, and working in unison to achieve shared goals set for the field. Many groups have already recognized the importance of collaborations, both domestic

and international. These groups have led the way in proactive advocacy for addressing ethical, legal, and societal implications in nanobiotechnology. If these collaborative priorities move toward the top of the list for funding and regulatory agencies, problems such as the Collingridge dilemma may be avoided all together.

Finally, it is important for society to differentiate between what is realistic and what is futuristic. Participating in discussions that are relevant to nanobiotechnology products that are close to production or already on the market is more tangible than arguing issues that are ahead of their time. This understanding will come from a variety of sources that influence peoples' views of nanobiotechnology, whether it is the news, popular media, or word of mouth. While stakeholders consider communication among themselves and improving the education of innovators in the field, the most important ethical consideration will be how to inform the public of the real-time science that is happening today, how it can affect their lives, and what role they can play in helping to advance nanobiotechnology safely and effectively.

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The Thorny but Pervasive Problem of Permissible Deaths

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ABSTRACT: This paper is concerned with the concept of “permissible deaths,” a difficult moral issue that ethicists, regulators, and policy-makers must deal with in a number of settings. In particular, the question as to how many “collateral damage” deaths are acceptable in the context of medical equipment design, the regulation of pharmaceutical products, and the conduct of war is discussed. I suggest that the various deontological approaches available are not helpful in analyzing this problem, primarily because they are intended to provide guidance against the causing of deliberate injury or harm, and do not provide guidance in the setting of unintended harm, as is the case in the permissible death problem. Similarly, the application of utilitarianism to this issue is problematic, because that would require that some kind of calculus be set up to assign specific values to various lost lives and injured parties in order to weigh them against various forms of benefit. In practice, this is an impractical task.

KEY WORDS: Björk-Shiley convexo-concave heart valve; cost/benefit analysis; doctrine of double effect; just war theory; permissible death; regulatory policy; risk; safety; utilitarianism

I. INTRODUCTION

Few legal drugs are used as ubiquitously as Tylenol, the popular, nonprescription analgesic known by the scientific name of acetaminophen (paracetamol in the United Kingdom). Although the use of acetaminophen is advocated for a number of mild-to-moderate pain conditions, such as headaches and arthritis, it is less well-known that in large doses acetaminophen can be lethal. In fact, acetaminophen liver toxicity, often from an intentional overdose, causes more than 450 deaths annually in the United States, and this number appears to be on the rise.¹⁻³ While there is little doubt that this number could be substantially reduced by restricting access to the drug, for example, by removing its nonprescription status or even removing the drug from the market entirely (as happened with the painkiller Vioxx), the fact is that regulatory authorities like the US Food and Drug Administration (FDA) must view this number of deaths as being acceptable in light of the enormous overall clinical benefits the drug provides. After all, if they didn't feel this way, they presumably would do something about it. This example illustrates the concept of “permissible deaths,” a thorny ethical issue that regulators and policy-makers must deal with in a great many settings.

The problem of permissible deaths is hardly unique to the regulation of drugs; there are many other instances where this nasty issue shows up. For example, generals conducting

military campaigns must decide how many combatant deaths on either side are tolerable, as well as decide how many unavoidable innocent civilian deaths are acceptable (“collateral damage”).^{4,5} Similarly, safety engineers must strike a balance between the cost of a safety feature and the number of lives saved, because, for example, relatively few people would be willing to buy a car costing \$300,000 no matter how safe.⁶ Likewise, adding numerous extra safety features to nuclear power plants, to commercial aircraft, or to invasive medical equipment could conceivably make these products too expensive to be affordable.

This issue even comes up in surgery. In high-risk procedures such as cardiac surgery, how many deaths are acceptable? In 1998, the British General Medical Council, the regulatory agency that monitors British doctors, charged that two heart surgeons under their scrutiny were guilty of operating on children despite knowing that their fatality rates were unacceptable.^{7,8} This naturally raises the issue as to what an acceptable death rate might be and how such a rate should be determined. In some states like New York, where the fatality rates for all heart surgeons are publicly available, one unintended consequence has been for heart surgeons to simply refuse to take on very high-risk cases for fear of adversely affecting their “batting average.”

Another medical situation concerns permissible deaths related to the use of medical equipment. For example, patient-controlled analgesia (PCA) machines, which allow patients to self-administer drugs such as morphine after painful surgical procedures, are inherently risky. While the potential benefits of this technology include superior pain control, automatic electronic documentation, and improved utilization of nursing resources, unfortunately, unanticipated flaws in the design of these machines can sometimes lead to adverse drug events such as overdoses and even death.^{9,10} One particularly notorious unit is the Abbott Lifecare 4100 PCA Plus II machine. In 1997, there were three documented deaths that occurred while the patients were connected to this device. Investigations revealed that part of the problem was an unfriendly user interface that made user errors more likely. Unfortunately, despite being amply notified of this problem, the manufacturer was unwilling to upgrade the unit to a safer design, claiming that there was no problem with the unit in the first place that could not be handled with proper user training. In the end, no design change was ever implemented and the unit remains in occasional clinical use to this day.¹¹

Clearly, complex technologies such as automobiles and nuclear power plants offer personal and social benefits at a price that necessarily produces occasional injury and death. Still, when government regulators license drugs or medical devices, they implicitly require that the perceived benefits exceed the perceived risks. In the case of drug products, when this relationship is no longer obvious, the drug may be withdrawn (as happened with Vioxx) or its indications restricted (as happened with Avandia). In the case of medical devices such as PCA machines, when preventable deaths or injury occur, the FDA may require that the device be recalled from clinical service so that safety upgrades can be instituted. However, as in the case of the Abbott PCA machine, this is not always the case.

Another example is the Björk-Shiley convexo-concave heart valve, an early-generation artificial heart valve that would occasionally fail catastrophically due to fracture of

a strut,¹² with as many as 480 deaths estimated to have occurred as a result. Because only a relatively small fraction of the approximately 80,000 implanted Björk-Shiley valves actually failed, not all valves were removed and replaced, because the comparatively small risk of valve fracture had to be balanced against the not-insubstantial risk and cost of the surgery needed to replace the valve.

Complicating this matter is the fact that, according to a US government lawsuit, the maker of the valve, Shiley Inc., issued false reports to the FDA both to obtain initial approval of the device and to keep the valve on the market. For example, Shiley did not inform the FDA that in some cases they polished, rather than rewelded, cracked valve struts in order to make them look normal in appearance. In 1986, the FDA stopped sales of the valve. By 1990, there were 100 lawsuits pending against the manufacturer.

Although the Björk-Shiley valve is an example of a product that the FDA acted on, authorities do not always take action against dangerous products. Failure to mandate a recall of medical devices that harm patients may occur for several reasons. First, the remedy may be so expensive as to be impractical. Second, the medical device may involve an old design that is approaching the end of its life cycle anyway. Third, regulatory agencies with limited resources must prioritize their goals, with the result that medical devices that injure or kill only a small handful of people may not get the regulatory attention that victims and their families would otherwise like. In such cases, legal remedies may be the only option available.

II. JUST WAR THEORY

The “Just War Theory” is a field of academic activity that studies the notion that armed conflict can and should meet specific criteria regarding the right to go to war (*jus ad bellum*) and regarding the proper conduct of war once hostilities have begun (*jus in bello*). For example, the Catechism of the Catholic Church¹³ lists four conditions for “legitimate defence by military force”:

1. The damage inflicted by the aggressor on the nation or community of nations must be lasting, grave, and certain.
2. All other means of putting an end to it must have been shown to be impractical or ineffective.
3. There must be serious prospects of success.
4. The use of arms must not produce evils and disorders graver than the evil to be eliminated.

The power of modern means of destruction weighs very heavily in evaluating this condition. Implicit to such considerations is the notion that military leaders must make every effort to plan their actions so as to reduce the chance of unintended injury or death, as well as to minimize accidental property damage. While accidental strikes against friendly or neutral forces is obviously undesirable, unplanned collateral damage against

enemy civilians and civilian facilities is usually also taken to be abhorrent.

With the advent of advanced computer-modeling techniques, military authorities are now able, at least in some scenarios, to arrive at precise numeric estimates for various kinds of collateral damage. This brings us once again to the question of exactly how many deaths are permissible in a particular situation. Not surprisingly, such considerations have occasionally resulted in substantial controversy.

III. DOCTRINE OF DOUBLE EFFECT

The “doctrine of double effect”^{14,15} is a principle of ethics potentially applicable in such settings. First espoused by Thomas Aquinas in his *Summa Theologica*, the doctrine states that it is sometimes permissible to cause a harmful side effect in bringing about a good end result, even though it would not be ethical to cause such a harm directly in order to bring about the same good result. According to the *Stanford Encyclopedia of Philosophy*,¹⁶ the doctrine “is often invoked to explain the permissibility of an action that causes a serious harm, such as the death of a human being, as a side effect of promoting some good end.”

As a case in point, the *Stanford Encyclopedia of Philosophy* goes on to provide the following example: “A doctor who intends to hasten the death of a terminally ill patient by injecting a large dose of morphine would act impermissibly because he intends to bring about the patient’s death. However, a doctor who intended to relieve the patient’s pain with that same dose and merely foresaw the hastening of the patient’s death would act permissibly.”

IV. PUTTING IT ALL TOGETHER: INVOKING MORAL THEORY

I would like to now spend some time discussing how moral theory might be applied to the scenarios described so far. Moral or ethical theory can be approached from many viewpoints.^{17,18} The deontological approach to morality (from the Greek word *deon*, or duty) is based on specific obligations or duties. These can be positive (such as to care for our family) or negative (such as not to steal). This approach is also sometimes called nonconsequentialist, because these principles are held to be obligatory regardless of any good or bad consequences that might result. For example, it is wrong to deliberately kill innocent people even if it results in great benefit.

In this context, the concept of the “categorical imperative” developed by the 18th-century German philosopher Immanuel Kant is highly relevant.¹⁹ Kant said that we must treat people as an end, and never as a means to an end, by which he intended that we should always treat people with humanity and dignity, and never use individuals as “mere instruments” toward our own happiness. Another version of the categorical imperative is to “always act in such a way that the maxim of your action can be willed as a universal law.”¹⁹

Other deontological approaches include “duty theory” (defining duties to God, duties to oneself, and duties to others) and “rights theory” (concerned with rights that all

people have, and which the rest of us must respect).¹⁷

It seems to me, however, that the various deontological approaches available to us are not particularly helpful in analyzing the permissible death problem. This is, I believe, because they are intended to provide guidance against the causing of deliberate injury or harm, but do not help us very much in the setting of unintended harm, which is the case for the permissible death problem. This leads us to consider whether a different category of moral theories, consequentialism, might be helpful to us.

In contrast to the various deontological approaches to morality, the consequentialist approach determines moral responsibility by weighing the consequences of one's actions.¹⁷ According to the consequentialist view, correct moral actions are determined by a cost-benefit analysis concerning the consequences of an action. Several subtypes of consequentialism have been proposed: i) the view that an action is morally correct if its consequences are more positive or favorable than negative to the person performing the action ("ethical egoism"); ii) the view that an action is morally correct if the consequences of that action are more positive than negative to everyone except the person doing the action ("ethical altruism"); and iii) the view that an action is morally correct if the action's consequences are more positive than negative to everyone ("utilitarianism"). It is this last view that I would like to discuss in more detail. Specifically, some philosophers might argue that a utilitarian approach would best fit most of the permissible death scenarios described above. They might even hold that it would form the basis for public policy in such matters, and this possibility is discussed next.

Utilitarianism is a school of moral philosophy frequently identified with the writings of Jeremy Bentham and John Stuart Mill.²⁰ In more recent years, it has undergone a number of refinements, such as the "preference utilitarianism" advocated by Professor Peter Singer.²¹ Classical utilitarianism advocates the principle of providing "the greatest happiness to the greatest number" as the basis for assessing the morality of various actions, while preference utilitarianism advocates the principle of meeting the preferences of the greatest number of people. Thus, good variously consists in providing maximal happiness (or satisfying people's preferences) and the rightness of an action depends directly or indirectly on its yielding such outcomes.

However, while utilitarianism has had a strong influence on the intellectual landscape of recent philosophical discourse, in particular in ethical theory, it is often seen to falter when it is applied to questions of social or individual justice. In particular, utilitarianism can sometimes violate common-sense notions of justice. Because utilitarianism seeks to maximize the total amount of a particular "utility" (like happiness or preferences) over a social group, it seeks whichever arrangement achieves maximum utility. But such an arrangement might be achieved by distributing benefits and burdens in a way that violates common notions of justice, as in the scenario where one innocent individual is killed to save the lives of many. Another example is that the use of slaves might greatly help to maximize the net happiness in a society, but common-sense notions of justice almost always take slavery to be wrong. Another criticism of utilitarianism is that under the goal of maximizing happiness or some other utility, the wishes and desires of

sadists and perverts are lumped in with the wishes and desires of everyone else when an overall determination of utility is made. A final issue, especially in the context of the permissible death problem, is that the application of utilitarianism in this specific setting requires that some kind of calculus be set up that assigns specific values to various lost lives and injured parties and weighs them against various forms of benefit. In practice, this is not a practical task.

Such issues led the philosopher John Rawls and others to take the position that we must reject utilitarianism and instead develop a genuine understanding of what is right and wrong as a basis for making ethical decisions. What is needed, Rawls argues, is moral theory with justice at its core.²² Unfortunately, Rawls' moral theory, at least as I interpret it, also seems to be unhelpful in dealing with the permissible death problem. As noted earlier, a unifying theory of ethical action that could be relied upon to provide precise guidance in all of the circumstances identified above would be very helpful. Unfortunately, it appears that no such universal approach is readily apparent. Instead, as with the approach the Catholic Church has taken in the case of Just War Theory, every situation must be judged on its individual circumstances. It will be no surprise to the reader, however, that in such cases reasonable individuals will frequently find themselves in disagreement with each other.

V. CONCLUSION

In conclusion, the concept of permissible deaths remains a thorny ethical issue that one encounters in a great many settings, covering issues as diverse as the regulation of drugs and medical devices to the debate about acceptable collateral deaths during the conduct of a "just war." Unfortunately, however, there is no single ethical theory that can be universally relied upon to provide practical guidance in all such settings.

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**ETHICS IN BIOLOGY,
ENGINEERING, & MEDICINE
AN INTERNATIONAL JOURNAL**

**Special Section:
Global Bioethics & The Reconvergence of Life Ethics**

**Special Guest Editor:
Daniel A. Vallerio**

The New Bioethics: Reintegration of Environmental and Biomedical Sciences

This special section is an expansive discussion of a wide swath of bioethical topics in the two most important public health professions: engineering and medicine. In fact, a number of the articles address what have become known as the “environmental health professions.” Engineers have designed systems to clean the air and water, to improve the safety of food, and to protect natural resources. Physicians and medical practitioners have treated and prevented diseases and are increasingly promoting the wellness of individuals and populations. A variety of environmental health scientists are helping to bridge these two disparate fields. Obviously, physicians and medical practitioners are the healers of our time. Unfortunately, few endeavors in the life sciences are without some costs and tradeoffs. This is the province of ethical decision making.

The term “bioethics” has lost some of its meaning since it was coined by Van Rensselaer Potter II (1911–2001) in the 1970s. It is now generally assumed to be a synonym for biomedical ethics, but the term originally conveyed a sense of integration and systematic thinking in all decisions related to living things. Thus, *Ethics in Biology, Engineering, and Medicine* is the ideal venue for retracing and reconstructing bioethics back to its comprehensive roots, which encompassed moral decision making regarding both medicine and the environment.

Potter considered bioethics as a bridge between the sciences and the humanities to serve the best interests of human health and to protect the environment:

From the outset it has been clear that bioethics must be built on an interdisciplinary or multidisciplinary base. I have proposed two major areas with interests that appear to be separate but which need each other: medical bioethics and ecological bioethics. Medical bioethics and ecological bioethics are non-overlapping in the sense that medical bioethics is chiefly concerned with short-term views: the options open to individuals and their physicians in their attempts to prolong life.... Ecological bioethics clearly has a long-term view that is concerned with what we must do to preserve the ecosystem in a form that is compatible with the continued existence of the human species.¹

This issue of *EBEM* includes a diverse group of authors who consider ethical decision making from numerous perspectives. Both the content and the conduct of science are addressed. What are some of the unique challenges of environmental research that involves human subjects? Are current investigations and conclusions adhering to well-established norms or are they drifting toward advocacy? Conversely, are we properly including all or even the correct members of the community so that our research is relevant and useful? Are the methods being employed ensuring good science or are there weaknesses due to conflicts of interest? Is privacy sacrificed inappropriately? How well are we teaching ethics within scientific subject matter, and what approaches would work

better? Are we truly respecting persons and providing proper autonomy, the best means of protecting health, and livable environments?

The march of the biological sciences has been justified as an overall benefit to humankind. However, this commitment and involvement calls for deliberate and serious considerations of actual and potential ethical issues. The President's Council on Bioethics² has summarized the dichotomy between the promise and ethical challenges:

... knowledge of how things work often leads to new technological powers to control or alter these workings, powers generally sought in order to treat human disease and relieve suffering. But, once available, powers sought for one purpose are frequently usable for others. The same technological capacity to influence and control bodily processes for medical ends may lead (wittingly or unwittingly) to non-therapeutic uses, including 'enhancements' of normal life processes or even alterations in 'human nature.' Moreover, as a result of anticipated knowledge of genetics and developmental biology, these transforming powers may soon be able to transmit such alterations to future generations.

Human health is inextricably tied to the environment. Therefore, the ethics of the life sciences must also be considered systematically in the search for proper means of intervention and prevention. Certainly, some of the challenges of medical practitioners and researchers are unique to their specialties. Neurosurgeons must make decisions about cognition, for example, when deciding on whether treating a disease is worth changes in personhood. However, many ethical challenges are shared by all life scientists. After all, medicine and engineering are working toward the same general objective: healthy people living in a healthful environment. Both professions apply the sciences to achieve this objective, albeit at different scales and complexity (e.g., physicians deal with one species and environmental scientists address many species). In this sense, this issue is all about ecology in a rather broad context. The authors are looking at how the life sciences can be used within the boundaries established by the scientific method to improve the public's health and welfare and how this can be done both morally and practically.

Some of the connections are rather obvious, such as the need for credible environmental studies of exposures of children to lead and mercury coupled with sound medical diagnosis and treatment of neurological problems, all the while respecting families and communities. This calls for analyzing the data in such a way as to assist the engineer and others in reducing or preventing exposure and changing the materials used in a product. Other connections are more indirect, or even obscure. For example, what will be the role of medical researchers and practitioners if climate change leads to the migration of tropical diseases? How certain must we be about the science before actions are taken to reduce the probability of expanded disease incidence?

Environmental and biomedical ethics are complicated because life is complicated. I tease my fellow engineers who happen to work in more abiotic disciplines (e.g., structural) that they enjoy much higher levels of precision and less uncertainty than those of us in the "bio" disciplines. Living systems are chaotic and messy.

Another challenge of life science ethics is that precaution does not precisely equal morality. In some cases, assuming the worst case is not tantamount to taking the ethical high ground. Unlike physicians, who are all in the business of biology, engineers may think of themselves as being in the business of physics, with the biomedical and environmental disciplines targeting this physics at living systems. While this is arguably true, all engineering is also “biotic” to some extent. Indeed, the engineer’s principal client is the public, so the structure must not only stand, it must serve a particular function. Every discipline must employ human factors engineering—not just answering the question of how something should be used, but also how it might be used. Do not be surprised at some of the novel (and dangerous) ways that something you design will be used, other than what you had thought would be its function.³ The point here is that outcomes will seldom follow a nice, linear path to the desired outcome. Sometimes, even a seemingly small, unaccounted for factor could result in an outcome no one expected or wanted. For example, if climate change is assumed to be drastic and calls for strict reductions in greenhouse gas emissions, could this stifle economic development and limit the opportunities for people to be lifted out of poverty? If we take a product off the market because it may damage the environment, but it is the only effective treatment of a debilitating disease, how did we weigh the risks and benefits to prevent greater human suffering?

This issue is devoted to considering such challenges in a systematic way. As is so often the case in ethical inquiry, there are many questions left unanswered. In fact, we may well have introduced more than we have resolved. I hope that reading these eclectic articles helps you to join the dialogue, and to extend it to all of the practitioners and researchers in the life sciences. Protecting human health and environmental quality calls for a proper consideration of attendant moral decisions. That is the goal of this EBEM issue. I would like to think that Potter would have agreed and may well have contributed.

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Science in the Sunshine: Transparency of Financial Conflicts of Interest

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ABSTRACT: Beginning in 1995, the U.S. Department of Health & Human Services (DHHS) issued conflicts of interest (COI) regulations to all institutional recipients of Public Health Service grants, including grants from the National Institutes of Health. These regulations set requirements for the disclosure and management of researcher financial COIs (FCOIs). In 2010, the DHHS revised its FCOI regulations. This paper reviews the historical conditions leading up to the first FCOI regulations and its revisions, discusses the response of journals to author COIs, and examines how well the revised regulations respond to criticism that grantee institutions were not properly managing FCOIs.

KEY WORDS: conflicts of interest; scientific objectivity; NIH, journal policies

I. INTRODUCTION

In May 2010, the U.S. Department of Health & Human Services (DHHS) proposed revised regulations, applicable to all grantee institutions and investigators, which set requirements for the disclosure and management of financial conflicts of interest (FCOIs). The new rules would be the first major revisions promulgated since 1995, when investigator-FCOIs were first regulated. In this paper I review the historical events leading up to current policies adopted by journals and federal scientific funding agencies on FCOIs. I discuss the trends among science and medical journals toward full disclosure of FCOIs by contributing authors and examine the changes in the newly proposed federal policy. Finally, I explore some shortcomings in the new proposed policy for achieving the government's goal of ensuring unbiased publicly funded scientific research.

II. HISTORICAL TRENDS

Concerns of FCOIs in the public sphere have their origins in the U.S. Constitution. The Founding Fathers, who had justifiable concerns that elected officials of the new Congress could be influenced by gifts or special favors, wrote into the Constitution some explicit prohibitions against egregious FCOIs. Article 1 forbids any person holding an office from accepting gifts, holding employment, or accepting titles from foreign governments without the consent of Congress. Also, no former member of Congress can assume a federal post that was created during his or her term of office.

Nearly 200 years after the ratification of the Constitution, Congress passed its most comprehensive regulations on COIs of government employees. The Ethics in Govern-

ment Act of 1978 established the Office of Government Ethics and created rules for financial disclosure for federal employees. Members of the upper levels of all three branches of government (including the president, vice president, members of Congress, federal judges, and certain staff members in each branch) must file annual public financial disclosure reports that list the sources and amount of all earned income; all income from stocks, bonds, and property; any investments or large debts; and the same information for spouse and dependent children. They must also report any positions or offices held in any business or nonprofit organization whether or not they are compensated.

Scientists serving on federal advisory committees were largely outside of federal oversight until 1972. In that year, the Federal Advisory Committee Act (FACA) was passed. Scientists serving on what currently amounts to about 1000 federal advisory committees are considered special government employees. According to FACA, no individual appointed to serve on an advisory committee can have a COI that is relevant to the functions to be performed, unless the conflict is promptly and publicly disclosed and the National Academies of Science determines that the conflict is unavoidable. It is now standard practice for scientists participating on federal advisory committees to disclose their competing interests at the start of their service. By the early 1980s, there was a significant cultural shift in academic science that brought COI concerns of the public and the scientific community to a new level.

At the start of the decade, a series of laws, executive orders, and tax policies designed to improve U.S. competitiveness in high technology were enacted and adopted. These policies were premised on the idea that if closer ties were developed between universities and industry, the rate of discovery would increase, technology transfer would expand rapidly, and the resulting innovations would create new industrial sectors and new wealth. Included in this new policy initiative were the enactments of the Bayh-Dole Act, the Stevenson-Wydler Technology Innovation Act, new tax policies, and Executive Order 12591 that stimulated university-industry partnerships. These policies gave universities and industry intellectual property ownership to discoveries funded by the government, tax credits to companies that contributed equipment to universities, tax incentives for limited partnerships between companies and universities, and funding for the formation of university-industry research centers at the National Science Foundation.

In 1980, *Nature* magazine asked a series of questions about the unintended consequences of those policies: “As industrial corporations become more involved in developing new biological techniques, where does this leave the scientist? How will university biology departments maintain their integrity and autonomy? How will individual scientists react to corporate demands?”¹ Journal editors, the so-called gatekeepers of certified knowledge, were among the first to respond.

III. MEDICAL JOURNALS: FIRST RESPONDERS TO AUTHOR COIS

By the mid-1980s, two leading medical journals introduced FCOI disclosures for authors. *The New England Journal of Medicine's* editor-in-chief, Arnold Relman, wrote an editorial in the journals titled “Dealing with Conflict-of-Interest,” which was a path breaker for

the medical journal community. Relman explained the reasons behind the new policy:

...in recent years, as the commercial possibilities of the new biomedical discoveries have become increasingly attractive, these connections [between industry and academic medicine] have become more pervasive, complex and problematic. Now, it is not only possible for medical investigators to have their research subsidized by businesses whose products they are studying, or act as paid consultants for them, but they are sometimes also principals in these businesses or hold equity interest in them.²

The very first journal policy was nothing more than a suggestion to authors that they list any funding or direct business interests that they considered to be related to the subject matter of their submitted article. Other types of FCOIs, such as patents and business consultancies, were a lower priority for the journal, which made a commitment to handling them on a case-by-case basis.

As the print media and Congress brought more attention to the links between academic scholars and industry, especially in drug research, the leading medical journals incrementally deepened and broadened their disclosure policies. Initially applied to original research, disclosure of FCOIs was extended in many journals to editorials, commentaries, meta-analyses, review articles, and book reviews. Some journals banned authors with FCOIs from publishing certain types of articles for which author bias was more difficult to detect, such as reviews of a field and commentaries.

For 6 years (1996–2002), the *NEJM* adopted a policy that prohibited editorialists and authors of review articles from having an FCOI with a company that could benefit a drug or medical device discussed in the article. In 2002, Editor-in-Chief Jeffrey Drazen withdrew the zero-tolerance policy and replaced it with a de minimis FCOI requirement applying a “significant conflict-of-interest standard” that was used to exclude certain authors from publishing in the journal.

Medical journals, more visible to the public through the eye of the media than journals in other fields, were the first to take FCOIs seriously. The general science journals followed their lead. After an initial resistance to requiring authors to make their FCOIs known to readers, the *Nature* journals were the last holdouts of the high-impact science journals to adopt a disclosure policy. In 1997, the editors of *Nature* wrote defiantly:

This journal has never required that authors declare such affiliations, because the reasons proposed by others are less than compelling. It would be reasonable to assume, nowadays, that virtually every good paper with a conceivable biotechnological relevance emerging from west and east coasts of the United States, as well as many European laboratories, has at least one author with a financial interest—but what of it? ... The work published (Science and Engineering Ethics 2, 395; 1996) makes no claim that the undeclared interests led to any fraud, deception or bias in presentation, and until there is evidence that there are serious risks of such malpractice, this journal will persist in its stubborn belief that research as we publish it is indeed research, not business.³

Four years later with the same editor-in-chief, the journal reversed itself and reached the decision to adopt a disclosure policy for author competing interests. Editor-in-Chief Philip Campbell wrote: “There is suggestive evidence in the literature that publication practices in biomedical research have been influenced by the commercial interests of authors.... There are circumstances in which selection of evidence, interpretation of results, or emphasis of presentation might be inadvertently or even deliberately biased by a researcher’s other interests.”⁴ Campbell was referring to the growing evidence that private funding of science had a biasing influence on its outcome.⁵ A study of 47 refereed toxicology and 180 medical journals found that 87% and 84%, respectively, had written COI policies for authors in 2009.⁶

IV. FEDERAL FUNDING AGENCIES ISSUE COI RULES

After a 10-year period during which scientific and medical journals were developing FCOI disclosure policies, two major federal science agencies, the Public Health Service (PHS), which includes the National Institutes of Health, in conjunction with the Office of the Secretary of DHHS and the National Science Foundation issued regulations after a year of public debate and input. The final rules were promulgated in 1995. In essence, this was a decentralized, locally managed system for addressing scientific COIs for investigators who received federal grants with federal walk-in rights to obtain information.⁷ Under the 1995 rules, faculty were required to report external income to a designated agent at their university. Much of that information was not available to the general public, researchers, or the media, but could be accessed by federal funding agencies at their request. .

For the purpose of the FCOI rules the DHHS defined “significant financial interest” (SFI) as anything of monetary value including consulting fees, honoraria, equity interests, and intellectual property that exceeded \$10,000 over a 12-month period.⁷ The reporting requirement excluded any salary or royalties from the applicant’s institution; income from seminars, lectures, or teaching engagements sponsored by public or non-profit entities; and income from an applicant’s service on advisory committees or review panels for public or nonprofit entities. The definition of SFI was designed to capture ancillary income from profit-making organizations that included the investigator’s spouse and dependent children.

The institution’s responsibility under the 1995 rules was to maintain and enforce a written policy and establish guidelines on COI, to ensure that investigators who receive PHS grants follow the policy and guidelines, to designate an official to solicit and review financial disclosures from those awarded these grants, and to take the appropriate action for managing, reducing, or eliminating significant FCOIs.

The institution must also report to the DHHS the “existence of a conflicting interest (but not the nature of the interest or the details) found by the institution....”⁷ They must assure the DHHS that a significant COI is managed properly. While the institution must make information available to DHHS upon request, it is not obligated to disclose the SFIs to the press or the public.

The federal compliance mechanism is triggered when two conditions occur: first, when an investigator fails to comply with the institution's COI policy, and second, when an investigator's non-compliance "has biased the design, conduct, or reporting of the PHS-funded research..."⁷ The burden is on the institution to show that both conditions apply before DHHS will undertake action on compliance. The system was based largely on the trust of institutions and investigators. NIH took little oversight responsibility.

V. THE INSPECTOR GENERAL: DEFICIENCIES IN OVERSIGHT

In January 2008 the inspector general (IG) of the DHHS completed his report on the number and nature of FCOIs reported by grantee institutions to the NIH, and on the extent to which NIH oversees its grantee institutions' FCOIs.⁸ The investigation had two goals: first, to determine if NIH kept an accurate accounting of the reported FCOIs, and second, to ascertain the extent to which NIH oversees grantee institutions' FCOIs. The IG found two deficiencies in NIH's oversight of the rules on COIs at grantee institutions. First, the NIH could not give the IG an accurate account of the FCOI reports for FY 2004–2006. Nearly half of the institutes could not provide the IG with any financial disclosure reports for FY2004–2006. Second, the IG felt that there was insufficient information about the COIs that were reported: "NIH is not aware of the types of financial conflicts of interest that exist within grantee institutions because details were not required to be reported and most conflict-of-interest reports do not state the nature of the conflict."⁸

As previously noted, the 1995 rules did not require the grantee institutions to report on the specific nature of the FCOIs, so it was not surprising to learn that "at least 89 percent of financial conflict-of-interest reports did not state the nature of the conflicts or how they would be managed."⁸ Only 30 of the 438 FCOI reports provided by NIH and reviewed by the IG included detailed information.

Another finding of the IG was that the individual institutes did not have a proactive method for ensuring that institutions had FCOI policies or for checking the accuracy and quality of the reporting by grantee institutions. It was based mostly on good faith. In response to the IG report, NIH did not agree that it should require grantee institutions to provide details on the FCOIs they report. The NIH director argued that such information should remain with the institution.⁸

VI. CONGRESSIONAL OVERSIGHT

In April 2007, Iowa Senator Charles (Chuck) Grassley hired Paul D. Thacker after Thacker had resigned as news reporter for *Environmental Science & Technology* (EST), an American Chemical Society magazine. While at EST, Thacker had written a number of articles about COIs in the biotechnology sector. It was after he honed his investigative journalistic techniques on the corporate influence on environmentally related science, fields such as energy and chemicals, that he began running into opposition from the EST board and editors. Thacker wrote a story in EST about the Weinberg Group, a scientific

consulting firm operating in Washington, DC hired by chemical companies to create uncertainty about scientific claims regarding the health and environmental effects of chemicals such as Teflon. He raised issues about whether environmental health science was for sale to the highest bidder. This brought Thacker criticism from EST for allegedly lacking proper training in investigative journalism and for failing to be balanced in his coverage of a story.⁹ After his magazine editor limited his coverage of certain topics, Thacker submitted his resignation and accepted a position with Senator Grassley, a ranking member of the Senate finance and budget committees, to work on the senator's investigative oversight projects.

Thacker began investigating the reporting mechanism of universities in response to FCOIs. He discovered a number of cases where there was a significant discrepancy between what a university professor claimed to report and what drug companies disclosed that they had paid the individual for consulting services. Based on Thacker's investigations for Senator Grassley, in June 2008 the *New York Times* reported "Researchers Fail to Reveal Full Drug Pay."¹⁰ The *Times* wrote that Senator Grassley found egregious violations in federal COI reporting requirements. They cited a Harvard child psychologist who promoted the use of antipsychotic medicines in children while earning at least \$1.6 million over a period of seven years of consulting.

Grassley wrote on his website: "We all rely on the advice of doctors, and leading researchers influence the practice of medicine.... Taxpayers spend billions each year on prescription drugs and devices through Medicare and Medicaid. The National Institutes of Health distributes \$24 billion annually in federal research grants. So the public has a right to know about financial relationships between doctors and drug companies."¹¹

With the support of Paul Thacker's findings that prominent NIH awardees failed to disclose consulting or equity income and thus flagrantly violated federal regulations, Senator Grassley began a two-year campaign to tighten up the rules and improve their oversight both at the NIH and at the awardee institutions. He wrote to NIH Director Elias Zerhouni on June 4, 2008 expressing his concerns about the management of COIs in NIH-supported institutions. Director Zerhouni responded on June 20 in agreement that "we need to increase transparency and enhance NIH's system of oversight" and that he was hopeful "that we can significantly enhance identification and management of FCOIs to insure that undisclosed, and therefore unmanaged, conflicts do not bias the design, conduct, or reporting of NIH-supported research."¹²

On June 25, 2008, Grassley wrote to the chair (Robert C. Byrd) and ranking member (Thad Cochran) of the powerful Senate Committee on Appropriations alerting them to the problems at NIH and the need for accountability and greater transparency. Grassley wrote, "As you know, institutions are required to manage a NIH's grantee's conflicts of interest. However, I am discovering that these regulations may be nothing more than words with little if any teeth." Citing the 2008 DHHS Inspector General report (see next section), Grassley teamed up with Senator Herb Kohl and on July 7, 2009 issued a press release urging NIH to take steps to increase transparency of federally funded biomedical research. They filed amendments into new legislation that would have placed new

requirements on institutions receiving NIH grants.

As a ranking member of the Senate Committee on Finance, Grassley issued press releases supporting changes in the NIH's COI policies. In one release he was quoted: "Letting the sun shine in and making information public is basic to building people's confidence in medicine. And with the taxpayer funding that's involved, people have a right to know. Public trust and the public dollars are at stake."¹³

During the confirmation hearings of Governor Kathleen Sebelius, seeking to be secretary of Health and Human Services, Grassley posed a series of queries to the candidate outlining the problems that he had identified and requesting her response. Sebelius' answers, while expectedly somewhat vague, did agree with the principles that Grassley had raised. "I support NIH's efforts and agree that it is time to reevaluate the existing FCOI regulation to assure that PHS supported research is conducted without bias."¹⁴

While building support from members of the Senate and keeping the pressure on DHHS and NIH by requesting data and urging policy change, Grassley continued to request information from universities in those cases where awardees had neglected to make proper disclosures. His efforts to raise visibility on COIs were greatly reinforced by two investigations of the IG.

VII. IG REVIEWS DHHS RULES ON COI

In January 2008, the IG issued the final report of its investigation on the number and nature of financial COIs reported by grantee institutions to the NIH, which sought to ascertain the extent to which NIH plays an oversight role in ensuring that its grantee institutions abide by the 1995 rules of reporting, managing, and mitigating FCOIs.¹⁵ The IG reviewed 438 reports and found a number of deficiencies in FCOIs in NIH grantee institutions. Prominent among them is that the IG could not obtain an accurate count of the FCOI reports for FY2004–2006; 93% did not state the nature of the conflicts; 89% did not state how the conflicts would be managed, reduced, or eliminated.

This latter point about whether the NIH should require detailed records of the types of COIs occurring at its grantee institutions became contentious between the agency and the IG. The 1995 rules did not require any level of detail in the reporting by grantee institutions to the NIH. The IG wrote: "At least 89 percent of financial conflict-of-interest reports did not state the nature of the conflicts or how they would be managed."¹⁵

The IG also found that individual institutes did not have a proactive method of ensuring that grantee institutions had FCOI policies, or if they did, the accuracy and quality of the FCOI information. Nearly half of the institutes could not provide the IG with any financial disclosure reports for FY 2004–2006. According to the IG report, the quality of the information was based mostly on "good faith." NIH responded to the IG report by disagreeing that it should require grantee institutions to provide details on the FCOIs they report. In essence, by demurring, NIH refused to take on a policing role of its grantee institutions, but rather preferred that the information be decentralized and based on trust.

The IG issued a follow-up report in 2009 titled "How Grantees Manage Financial Conflicts of Interest in Research Funded by the National Institutes of Health."¹⁶ The IG

cited inquiries of the Senate Finance Committee into payments from drug and device manufacturers to academic researchers and physicians. In nine cases, they found five awardees who allegedly failed to report that they received payments of \$1 million or more. In this investigation the IG reviewed 41 grantee institutions that submitted 225 FCOI reports to the NIH in FY2006. These institutions were surveyed on how FCOIs were managed, reduced, or eliminated and how grantee institutions ensured that their researchers complied with federal regulations. After excluding 41 grantee institutions from its analysis, the study was left with 184 reports involving 165 researchers. The most common type of conflict that the IG found among researchers (67%) was “holding an equity ownership” in companies whose financial interests were related to the investigator’s research, while 40% of the grantees consulted for an outside company. Sixty-five grantees had some type of position with outside companies including executive office and membership on the board of directors, advisory board, or medical review board.

Of the 184 reports, 136 indicated that the researchers’ conflicts were managed, six indicated that the conflicts were reduced, and a mere six were eliminated.¹⁶ The most cited method for managing COIs was disclosure. And for one-third of the reports (n = 60), there was no evidence in the submitted documentation to show that management methods were fulfilled.

Once again, the IG report confirmed that “researcher discretion” in deciding what to report guided the management plans. “Ninety percent of the grantee institutions rely solely on the researchers’ discretion to determine which of their significant financial interests are related to their research and are therefore required to be reported.”¹⁶ The IG also reported that none of the grantee institutions have a policy of full disclosure of SFIs, but rather allow the researcher to make the determination of whether disclosure is appropriate. Most of the institutions do not make an effort to verify information submitted by researchers.

The IG recommendations in the second report once again focused on the lack of detail in the information sent to NIH from grantee institutions. The IG recommended that “after a grantee submits a report identifying the existence of a conflict, NIH use [its authority] to request details about the conflict and how it was managed, reduced or eliminated.”¹⁶ The IG also criticized the investigator “trust standard” in the reporting of FCOIs and recommended that “NIH require grantee institutions to collect information on all significant financial interests held by researchers and not just those deemed by researchers to be reasonably affected by the research.”¹⁶ Under these criteria, all external income that exceeds the threshold would be reported.

VIII. REVISED PHS RULE ON REPORTING FCOIS.

The DHHS issued a new set of proposed rules pertaining to COIs in academic research on May 21, 2010.¹⁷ The goal set forth by DHHS in this proposed rule was to ensure objectivity in funded research. To fulfill this goal, institutions and investigators had to completely disclose COIs, develop appropriate review of faculty with FCOIs, and aggressively manage the conflicts that are disclosed. DHHS stated that the 2010 proposed

rules represent “substantial revisions to the current regulations.”¹⁷ Many of the proposed revisions were direct responses to the IG recommendations and to Grassley’s campaign for change.

The proposal changed the definition of “financial interest” from “anything of monetary value” to “anything of monetary value or potential monetary value.” The new rules would require awardees to report intellectual property and equity in a startup company, which currently may have no monetary value. The new rules broaden the meaning of *investigator* to include anyone who is responsible for the design, conduct, or reporting of research, including sub-grantees and contractors, and *research* as any activity for which research funding is available, including PHS awards, grants, cooperative agreements, contracts, or career development funds.¹⁷

The definition of an SFI in the document is “a financial interest consisting of one or more of the [financial] interests of the Investigators (and those of the Investigator’s spouse and dependent children) that reasonably appears to be related to the Investigator’s institutional responsibilities.”¹⁷ The interests include stock holdings, remunerations from companies that aggregate within 12 months to more than \$5000, and intellectual property such as patents and royalties.¹⁷ Thus, the new rules cut the reporting threshold for external funding in half, from \$10,000 to \$5000. If an investigator holds an equity interest in a non-publicly traded company (i.e., a startup) then an SFI would exist regardless of the value. Also, there was a change in the time period under which the SFIs aggregate. Under the 1995 rule, aggregated payments were supposed to be calculated “over the next 12 months,” whereas under the new rules, they are calculated over the past 12 months. If investigators receive external monies that meet the SFI threshold after their disclosure statement has been made, they are required to update their statement within 30 days.

The new definition of SFI also introduces new criteria for disclosing some activities as SFI. In the past rules, the external funding had to be related to the current PHS grant. The new rules state that disclosure is required for any external funding classified as SFI that would “reasonably appear to be related to the Investigator’s ‘institutional responsibilities.’”¹⁷ This means that institutions must disclose external funding classified as SFIs that relate to any aspect of an investigator’s scientific life, including teaching at the institution.

In what is likely to be the most controversial changes to the current federal COI policy are the institutional requirements for record keeping and reporting of FCOIs. Institutions will be required to post their COI policies on a publicly accessible website, to develop and implement training programs on their policies, and to require all PHS investigators to complete the training. Up to now, the investigator bore the responsibility for determining the relatedness of the SFI to his or her PHS-funded research. Under the proposed rules, it is the institution’s responsibility, through a pre-designated office, to make the relatedness determination. When a determination of SFI and its relatedness to an investigator’s work has been made, the past rules required the institution to manage the conflict, while the new rules would require the institution to create a management

plan to be submitted to the awarding agency.

Standing out among the institutional changes is the new public disclosure provision. When an institution has determined that an SFI of a senior investigator or key personnel of a PHS-funded project is related to the research, and that it involves an FCOI, then the institution is required to post information describing the FCOI on a publicly accessible website. This means that some investigators will have personal information about earnings and their (and their family's) financial relationships with private companies made public. The publicly accessible website would be updated annually or within 60 days of a change in the SFI status of an investigator. The DHHS discussion of the proposed guidelines noted the significance of the change to personal privacy. "We recognize that the proposed public disclosure requirement would place an additional administrative burden on institutions, and would also impact the privacy of Investigators who have information related to their personal financial interests posted publicly to the extent such interests are determined to be FCOI."¹⁷ In balance, DHHS noted, the publicly accessible website has the advantage of offering the public more complete information; it is also consistent with public disclosures in journals and at professional meetings.¹⁷

The problem associated with poor compliance of the regulations was a major factor in bringing public attention to the 1995 COI policy. Under the old rules, if an investigator failed to comply, the institution was required to inform PHS of the action it planned to take or had taken. The new rules expand the power of investigation of the awarding agency. The agency would be able to undertake a site review before, during, or after the award period, gain access to all relevant records of the awardee institution, and exercise enforcement action that includes suspension of funding or imposing special award conditions. The new rules stipulate that greater enforcement attention is given to research that evaluates the safety or effectiveness of drugs, medical devices, or treatment.

While remaining within the same general framework as the existing rules, the proposed rules on COI provide greater detail, close up loopholes in reporting, provide greater transparency to the public, shift responsibility from the investigator to the institution, and establish higher accountability standards for the awarding institution.

IX. CONCLUSION

The 2010 proposed DHHS rules on COIs have responded to most of the criticisms and recommendations issued by public critics, Senate oversight committees, and the IG. Some highly visible cases have illustrated the extent to which some academic scientists and their institutions treated the 1995 rules as burdensome and intrusive. Some members of this group of scientists felt emboldened to flaunt the rules, which they viewed as needless regulatory impositions on science that erodes their established tradition of "academic freedom and autonomy."

Under the newly proposed rules, Senator Grassley's idea of "science in the sunshine" is extended from journal disclosure to all grantees of PHS awards. Transparency is now required, at least for publicly funded research, at the outset of receiving an award and not just at the time of publication. This gives the university an opportunity to raise

the question of whether the investigator's significant FCOI could bias the results of the research. However, even with the revised rules, there remain significant omissions in addressing FCOIs in science.

First, we have to acknowledge that a significant funding of science, particularly as applied medical research, comes from the private sector. Investigators who do not receive public funds are not bound by the DHHS rules. Private funding of academic research has introduced systemic bias, perhaps more directly than public funding.¹⁸ The bias is often introduced at the outset in the contract of the study. For example, recently it was disclosed that the international energy corporation BP proposed to contract out research to scientists at the University of Alabama, which would have given the company rights over publication. According to a report in the *Press Register* of Mobile, Alabama, BP attempted to hire the entire marine sciences department at one Alabama University under a contract that "prohibits the scientists from publishing their research, sharing it with other scientists or speaking about the data that they collect for at least the next three years."¹⁹

Second, improving the management and disclosure of COIs does not solve the problem of prevention.²⁰ The introduction of bias in research can be very subtle. It is not easy to determine whether an SFI biases the outcome of research unless there are telltale clues. The policy sets no boundaries on preventing an FCOI, such as by prohibiting a clinical investigator supervising a clinical trial from holding an FCOI.

Third, the DHHS's proposed rules do not address the problem of institutional COIs, which the agency has thus far found intractable. It is the universities who may negotiate contracts with secret covenants that trade off scientific autonomy in exchange for large grants or other largesse to the institution (including equity interests in the funder) that makes this issue so visible yet beyond the management of investigator COIs.

Finally, the newly proposed DHHS guidelines would replace the original guidelines, which have been in effect for 15 years. The new guidelines herald a new age of science, one in which "disinterestedness" as formulated by Robert Merton in his norms of science, is replaced with "managed bias," namely, an acceptance that science is largely influenced by entrepreneurship and that all there is left is to maximize the use of "organized skepticism" and transparency to ensure the publication of reliable knowledge. It broadens the responsibility from journals and the community of scientists to officers at the university who must decide whether "there is any reasonable expectation that the design, conduct, or reporting of PHS-funded research, by any investigator FCOI will be biased by the financial interest of that investigator."¹⁷

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Protecting Privacy and Confidentiality in Environmental Health Research

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ABSTRACT: Environmental health researchers often need to make difficult decisions on how to protect privacy and confidentiality when they conduct research in the home or workplace. These dilemmas are different from those normally encountered in clinical research. Although protecting privacy and confidentiality is one of the most important principles of research involving human subjects, it can be overridden to prevent imminent harm to individuals or if required by law. Investigators should carefully consider the facts and circumstances and use good judgment when deciding whether to breach privacy or confidentiality.

KEY WORDS: privacy; confidentiality; environmental health research; ethics; home; workplace; informed consent

I. INTRODUCTION

Environmental health scientists frequently conduct research on exposures to pesticides, allergens, industrial chemicals, and other substances in the home or workplace, which can provide valuable information for preventing diseases and promoting health.¹ For example, studies of exposure to allergens in the home provide useful information for preventing or managing respiratory diseases such as asthma.² Research on pesticide exposure of agricultural workers can help public health professionals to develop interventions for preventing pesticide poisoning and reducing the risks of developing illnesses (e.g., Parkinson's disease) related to long-term pesticide exposure.³ However, research on domestic and occupational exposures can pose ethical dilemmas related to the protection of research subjects or others, because investigators may ask individuals for information pertaining to private behaviors such as substance abuse or sexuality, or they may collect samples from private areas such as bedrooms, bathrooms, or offices. Investigators may inadvertently discover information related to illegal or illicit conduct such as child abuse or violations of occupational safety laws.¹ Therefore, environmental health researchers often need to make difficult decisions about how to protect privacy when they conduct research in the home or workplace.¹ These dilemmas are different from those normally encountered in clinical research.

II. PRIVACY AND CONFIDENTIALITY

Privacy and confidentiality are related but different concepts. Privacy refers to an individual's interest in controlling access to himself or herself.⁴ There are two distinct types

of privacy: informational privacy and physical privacy. Informational privacy refers to the interest in controlling access to private information about one's self, such as data pertaining to medical conditions, sexual practices, income, or social security number. Physical privacy refers to the interest in controlling access to one's body, biological specimens, or personal space. Observing a person undressed without permission would be an invasion of that person's physical privacy but not necessarily his or her informational privacy. Illegally accessing a person's medical records would be an invasion of informational privacy but not necessarily physical privacy. Confidentiality refers to measures that are taken to protect an individual's informational privacy, such as limiting access to medical or research records, data encryption, and secure data storage.⁴ Confidentiality is concerned with informational privacy, not physical privacy.

Many philosophers have examined the moral foundations of privacy interests. Some hold that the obligation to protect privacy is ultimately based on other, more fundamental moral principles such as the right to liberty or autonomy or the duty to not harm others.⁵ For example, breaching medical confidentiality can be regarded as unethical because it can cause harm such as loss of employment, discrimination, legal liability, or embarrassment to the person. Breaching confidentiality may be unethical even if it does not cause any harm because it violates a person's right to control the disclosure of private information. Watching someone undress without permission invades physical privacy; even if it does not cause harm to the person, it violates his or her right to control access to his or her body. Others hold that violations of privacy are wrong because they undermine intimacy, which is necessary for the formation of meaningful human relationships. People develop close relationships by sharing private information, secret dreams and desires, and physical space. Because people cannot form these close relationships unless they have some expectation that their privacy will be protected, society needs laws and ethical rules to protect privacy.⁶

A. Protecting Privacy and Confidentiality in Research Involving Human Subjects

Regardless of how one understands the moral foundations of privacy, it is clear that privacy and confidentiality are important values that should be protected in research with human subjects.⁷ Numerous ethical codes and legal mandates, such as the Declaration of Helsinki,⁸ the Council for the International Organization of Medical Sciences guidelines,⁹ and U.S. federal research regulations,¹⁰ require investigators to protect the privacy and confidentiality of research participants and to explain how privacy and confidentiality will be protected during the informed consent process. Many commentators recommend that investigators should also protect the privacy and confidentiality of third parties who may be directly affected by research but who are not the subjects of research, such as occupants of a home in which data collection takes place, family members identified in genetic research, or communities participating in a study.¹¹ Additionally, state and federal laws that protect the privacy of patients receiving health care, such as the Health Insurance Portability and Accountability Act (HIPAA), also apply to research activities.¹²

In clinical research, investigators collect private information such as a person's medical and family history, sexual behaviors, alcohol and drug use, diet, exercise, clinical laboratory test results, genetics, and environmental exposures. Because clinical investigators rarely need to enter a person's home or office to collect this information, most of the privacy issues in clinical research center on safeguarding confidentiality.¹³ To be sure, difficult ethical dilemmas can arise when deciding how to protect confidentiality in the clinical setting, such as deciding whether to disclose a person's HIV status to affected parties, but these ethical dilemmas are different from those that arise in health research conducted in the home or workplace environment, because clinical researchers usually obtain this private information as part of their study, not inadvertently during data collection in a private area.^{1,14,15}

B. Protecting Privacy and Confidentiality in Environmental Health Research

When investigators conduct research in the home or workplace, they may request private information from research subjects, such as medical history, daily activities, diet, and drug and alcohol use. The ethical dilemmas concerning the protection of private information obtained as part of the study are similar to those encountered in clinical research. However, investigators may also discover private information that is not being collected as part of the study when they enter a home or workplace.^{1,14} For example, in a study of how allergens in the home affect asthma, investigators may collect dust samples from bedrooms, bathrooms, recreation rooms, dining rooms, hallways, kitchens, and basements. When investigators enter these areas, they may observe evidence of illicit drug use or other illegal activities, building code violations, dangerous conditions in the home, domestic violence, and child or elder abuse/neglect. In a study of how chemical exposure in the factory affect health, investigators may collect samples from offices, assembly lines, bathrooms, dining areas, locker rooms, waiting rooms, and hallways. When investigators enter these areas, they may observe evidence of illicit drug use, alcohol use, or violations of environmental and occupational safety laws.

Ethical dilemmas arise when investigators have to decide what, if anything, they should do with the private information that they inadvertently discover in a home or workplace. As we have seen, ethical guidelines and regulations require investigators to take steps to protect private information. However, investigators may sometimes have good reasons to override these obligations and disclose private information obtained in the home or workplace. The most compelling reason to disclose private information is to protect individuals, especially children or vulnerable adults, from harm. Most ethical theories hold that we should help other people when it is reasonable to do so, including taking appropriate measures to rescue people who face imminent harm.¹⁶ For example, if we see someone drowning in a pool, we should throw in a life preserver, call a lifeguard, or take some other measure to save the person's life. We need not jump into the pool to save the person unless we are trained in water safety because this would risk our own lives, but we should not stand by idly.

If an investigator discovers evidence of child abuse/neglect while collecting samples in the home, he or she would have a strong moral obligation to report that information to the relevant authorities to protect the child from harm. The investigator may also have a legal obligation to report evidence of child abuse/neglect, because many jurisdictions have laws requiring educators, health care workers, and members of certain professions to report child abuse/neglect.¹ However, there may also be reasons not to report suspected child abuse/neglect, such as in cases where the evidence may be inconclusive and reporting the situation to the authorities may cause unnecessary harm to the child or other family members.¹⁴ Investigators should carefully consider these and other facts and circumstances when deciding whether to report. They may also discuss the situation with the parents or guardians prior to taking any action if they believe there has been some misunderstanding.

Investigators may encounter reporting dilemmas when they collect samples in the workplace environment. For example, suppose that investigators observe significant violations of occupational safety laws in a factory that place workers in imminent danger. They would have a strong ethical obligation to report these violations to the appropriate authorities to protect the factory workers from harm. However, similar to the child abuse/neglect example, there may be reasons not to report workplace safety issues: the evidence may be inconclusive, the potential harm to employees may be minimal, some workers may be fired if a safety report is made, and the entire research project may be jeopardized if the employer decides to no longer cooperate with the researchers. To deal with these and other contingencies, investigators should discuss safety violations with the management before contacting outside authorities, because the information that is disclosed may be harmful or embarrassing to employers. It may be possible to resolve these issues in a way that protects workers but also does not harm the employer or undermine the study. Investigators should use good judgment when deciding how to approach workplace safety issues that they discover while conducting a study.

Other rationales for compromising privacy are less compelling than protecting people from imminent harm. For example, suppose that investigators discover evidence of illegal drugs in a home. One could argue that they should report this illicit activity to the police to help enforce the drug laws and protect residents of the home from the potential harm associated with drug use. However, reporting the presence of illegal drugs in the home could do more harm than good, because making a report may undermine the research subjects' trust in the investigators, the evidence may be inconclusive, and the police may decide not to investigate the complaint anyway. A great deal depends on the circumstances of the situation. For example, if the investigators discover only a small amount of marijuana on a shelf where they are collecting dust samples, perhaps they should not say anything. However, if the investigators discover a large cache of various illegal substances, which would indicate that someone is selling drugs on the premises, and there are children in the home who may be in danger as a result of this illegal activity, then they should consider making a report. Once again, investigators should use good judgment when deciding whether to report illegal drugs (or other illicit activities)

in the home and they should carefully consider the relevant facts. They may also discuss these issues with occupants, if appropriate.

Investigators may also encounter situations in the workplace that do not necessarily require them to make a report to the relevant authorities. For example, suppose investigators discover potential violations of environmental laws when collecting data in a workplace. If these violations do not place people in imminent danger or pose significant, imminent risks to the environment, then they may decide to discuss the issue with the management rather than making a report to the authorities. Other illegal activities discovered in the workplace, such as evidence of alcohol/drug abuse, sexual harassment, or fraud/embezzlement, may be treated in a similar fashion.

The informed consent process can play a critical role in addressing issues related to privacy, confidentiality, and reporting illegal or dangerous activities to authorities.¹ Federal research regulations¹⁰ and other ethics rules⁹ require investigators to inform research subjects about how confidentiality and privacy will be protected. Investigators should not only notify subjects about measures that will be taken to safeguard confidentiality and privacy, but they should also inform them about circumstances in which they are obligated to breach confidentiality or privacy, such as reporting child neglect/abuse. Because it will not be possible to anticipate every situation in which it may be appropriate to breach confidentiality or privacy, a generic statement such as “privacy or confidentiality may be breached to protect people from imminent harm or if required by law” may be appropriate. Investigators should also discuss potential privacy/confidentiality issues with employers when conducting a study at a worksite. Talking about these issues with research subjects and other affected parties can help to promote trust and cooperation and avoid misunderstandings.

Investigators should also address privacy and confidentiality issues when planning a research project and developing a protocol. They should clearly describe the steps they will take to protect privacy and confidentiality, and how they will handle situations in which they may have an ethical or legal obligation to breach privacy or confidentiality. They should describe these issues in sufficient detail so that an institutional review board or other ethical review committee can understand how the proposed research project will affect the rights and welfare of human subjects and other affected parties, and how the investigators plan to protect them.

Finally, it is important for investigators to train research staff about privacy and confidentiality issues that may arise when collecting data in a home or workplace.¹⁴ They should inform research staff about the measures that will be taken to protect privacy and confidentiality, such as secure storage of research records, limited access to data, and encryption, and instruct research staff on the importance of avoiding unnecessary invasions of privacy in the home or workplace. For example, research staff should not open drawers or closets without permission, and they should not snoop around the home or workplace. They should collect samples only in pre-approved, designated areas. They should also be instructed on what to do if they inadvertently discover illegal or dangerous activities. Training may need to be revised as investigators acquire more experience in conducting research in the home or workplace.

III. CONCLUSION

Protecting privacy and confidentiality presents some unique—and often difficult—ethical dilemmas for investigators who are collecting data in the home or workplace environment. Privacy and confidentiality can be breached to protect people from imminent harm or if required by law. Investigators should carefully consider the relevant facts and use good judgment when deciding whether to compromise privacy or confidentiality. They should also address these issues when developing a research protocol and during the informed consent process, and should train research staff on confidentiality and privacy protections and concerns.

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The Scientific Method in an Era of Advocacy

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ABSTRACT: The scientific method is the standard approach used in conducting experiments that seek to prove or disprove scientific hypotheses and theories. The roots and applications of the method are examined herein from a bioethical perspective. Examples are outlined throughout the discussion, and the methods of funded science are reviewed from the standpoint of the need for innovation and discovery. Current challenges to science and the application of the scientific method are presented as they relate the approaches employed to solving major scientific problems. The essay also provides some insights into the need to improve approaches for examining the value of the vast amounts of information being gathered in all areas of science and engineering before one attempts to draw conclusions on superficially analyzed data sets. The discussion concludes with observations and recommendations about the steps needed to ensure the role of the scientific method in discovery.

KEY WORDS: scientific method; ethics; science history; scientific revolutions; value of information

I. INTRODUCTION

Biomedical and environmental technologies and tools were developed using the principles and methods of science and engineering available since the Renaissance and accelerated during the first half of the 20th century. A growing question is whether this noble method will withstand the influence of external forces and whether it will be able to continue to drive new discoveries in various fields and push the envelope of science. For example, Horgan has articulated the means by which tacit and overt biases have crept into and diminished the credibility of science projects in numerous disciplines.¹ These troubling issues have become progressively more acute in light of recent trends and events that have placed scientific research increasingly within the belief systems of politics and ideologies.

Science strives to explain natural phenomena. When doing so, scientists gain, or at least attempt to gain, power over the entity being investigated. Explaining the atom was necessary to control some aspect of its structure that led to its disintegration in the cyclotron. Describing how light behaves allows for ways to control it in a telescope or laser. Understanding how a molecule is structured allows for efficacious medicines and treatment of cancer. Indeed, the basic scientist may see “control” and “power” as motivators only for the applied sciences, but power and control are motivators for all science, albeit in different forms. Poincaré put it this way: “If nature were not beautiful,

it would not be worth knowing, and if nature were not worth knowing, life would not be worth living.”²

In this case, the teleology indeed is power and control. This is done, for example, by taking a part of nature and bringing into the laboratory to study, and it is driven by the “beauty” of science. Of course, the teleology of the applied scientists, engineers, and technologists is direct. Science provides them with the power to explain and *use* the knowledge for some noble (hopefully) purpose to improve society or the quality of life.

The scientific method has been debated throughout history, beginning with the ancient Egyptians and ancient Greeks (including Aristotle) and extending to more recent notables such as Karl Popper and Thomas Kuhn. The crucial aspects of the method are the formulation of a problem by hypothesis, followed by the collection of data. Modern science resulted from debates and disagreements of the intellectual giants of the 16th and 17th centuries. Indeed, Thomas Hobbes and Robert Boyle argued over the ground rules of truth seeking. Hobbes argued for a priori approaches, whereas Boyle and his ilk in the Royal Society felt that the only proper way to explain the physical universe is to take a rigorous path that includes experimentation, publication, and peer review. Hobbes lost that argument and, until recently, the scientific method has held primacy. Thus, the appropriate context for this essay in context begins by defining this durable method. The Merriam Webster Dictionary (ca. 1810) defines the scientific method as:

The principles and procedures for the systematic pursuit of knowledge involving the recognition and formulation of a problem, the collection of data through observation and experiment, and the formulation and testing of hypotheses. Empirical information can be used to test a theory which is considered the most direct (parsimonious) way to explain information from a body of data collected are consistent and can be synthesized to explain natural phenomena.

Scientific discovery is a cumulative process, with each discovery affected by previous successes and with each new discovery influencing all those to be made in the future. This march of science depends on collecting scientific information at each successive stage. However, while information gained from a discovery is a necessary, it not a sufficient requirement for scientific advancement. The layering of discoveries also needs to be viewed systematically to achieve coherence in thought.^{3,4} Science requires asking more than “what,” but also “why.” For the layers of observation to have meaning within the context of the universe, the explanation of natural phenomena must be based on the discovery of the theory behind a particular phenomenon and defining the basic principles that govern the processes. Boyle’s air pump certainly provided interesting data and information, but his discovery of “truths” regarding pressure, volume, and temperature only began to cross the theoretical threshold with Boyle’s Law. For every scientific law, however, there are countless wrong theories. Sifting through this morass of wrongheadedness requires adherence to a standard of intellectual honesty, as articulated by Snow: “The only ethical principle which has made science possible is that the

truth shall be told all the time. If we do not penalize false statements made in error, we open up the way, don't you see, for false statements by intention. And of course a false statement of fact, made deliberately, is the most serious crime a scientist can commit."⁵

Science is the explanation of the physical world, while engineering encompasses applications of science to achieve results. Indeed, societal demands can be very compelling. What has been learned about the environment by trial and error has been transformed into the more rigorous fields of biomedical and environmental science and engineering. However, it appears that in some cases the level of uncertainty in the collected data still are either not reported or are even intentionally ignored. Indeed, scientists may be tempted to speed up the process, to skip a step here and there, or even to embellish the real data to serve an important need, and therefore discussion and improved understanding of a phenomenon suffers. Heuristically attained knowledge has come at a great cost in terms of the loss of lives and diseases (e.g., popular yet wrong theories regarding physiological processes).

One of the principal values of the scientific method is its objectivity. The integrity of a scientist is determined by the extent to which a scientist's methods do not deviate from the standard. The method is also a defense against science and engineering activities becoming popularity contests or driven by the "pollutant of the day" or the "disease of the year."

Strict adherence to the scientific method can be a major inconvenience to a scientist's aspirations. Scientists can be recruited, sometimes unknowingly, as advocates for one cause or another. Many of these causes are worthwhile and policy makers are willing to fund them. Therefore, research funding today follows both scientific and policy-directed agendas. The temptation is to apply for funds and to write research proposals that fit what policy makers want; even if that means that the better and more relevant research will be in another area. It is seldom that the scientific community has 100% consensus on anything except the basic principles (and even these are suspect in quantum mechanics and mathematics). Science must be willing to go against the grain. Seldom is a scientific issue "settled," as has been reported recently regarding anthropogenic global warming.⁶ Indeed, there will often be a modicum of or even a general level of *consensus*, but not *unanimity* in any scientific discipline when the underlying theory is still evolving and the uncertainties still need to be reduced by experiment and observation. The thoughtful scientist must ask what exactly is supposed to be settled. For example, is there overall agreement that carbon dioxide and other greenhouse gases are one factor in how the earth is warmed by incoming solar radiation? Few scientists would disagree, since this is basic thermodynamics. Beyond these basics, however, the so-called settlement becomes friable, as evidenced by the disagreement about how to allocate the weights and inter-relationships of variables important in any heat engine or climatological process.

Sigma Xi, the Scientific Research Society, takes Snow's maxim one step further, noting that truth is the ultimate moral imperative of the scientist:

Semantic arguments apart, there remain two fundamental reasons why scientists should be concerned with the ethics of their research. The first reason is that

without the basic principles of truthfulness – the assumption that we can rely on other people’s words – the whole scientific research enterprise is liable to grind to a halt. Seeking the answers to questions may or may not be the cement that holds together society as a whole, but certainly it is essential to science. Secondly, whereas truthfulness in a wider context can be maintained and enforced by the institutions of the society we live in, scientific research is a specialized activity; namely, each scientist working largely on individual experiments and analyses on the fringes of knowledge.⁷

A. Scientific Revolutions and Paradigms

Scientific theories have risen and fallen with each “revolution” of knowledge. Kuhn⁸ warned the purveyors of scientific truths that to debunk current theories will be met with violent disagreement. Scientists do not relinquish their theories easily. Kuhn’s book provoked controversy and many years of discussion and other thought-provoking articles and books.⁹

During the turbulence of the 20th century—two world wars and an economic depression—scientists were also provided with a very rare opportunity to witness and appreciate the impact of multiple “revolutionary” discoveries and other types of advances in science, engineering, and technology. The two most acclaimed examples of scientific revolutions during the 20th century were the discovery of the theory of relativity in physics.^{10,11} and the double helix in biology¹²; each was an amazing theoretical advance in science: one employed the creative use of telescopes for proof and the other used the results from a sophisticated instrumentation for time (crystallography), respectively. Neither required the stamp of “peer reviewable” research prior to achieving the revolutionary discovery; however, both were built upon the successful application of the scientific method to describe various supporting phenomena that were observed or hypothesized by others.

Kuhn’s term “paradigm shift” described the post-revolution period in science.⁸ He defined “paradigm” as an accepted specific set of scientific practices made up of what has been observed and analyzed. A paradigm not only consists of laws and theories, but designates the gatekeepers of that field of study, those to whom questions should be asked, and how the results of the investigations into this specific subject matter will be interpreted. This gatekeeping aspect of the paradigm is perilous if incorrect theories and information become blindly accepted. Excessive comfort with the status quo or the fear of the different (i.e., xenophobia) can be sometimes attributed to a community’s well-organized protections against differences even in the face of legitimate dissent (i.e., “groupthink”).¹³

Until very recently, at least through the 19th century and the first two-thirds of the 20th century, major experiments in many areas of science and engineering were almost exclusively conducted by individuals in small, even obscure, laboratory settings. Examples include antibiotics, the Curies’ experiments on radium, and the Apple/Microsoft-based evolution of personal computer software. At times, innovations occur when a

need or opportunity arises. “Necessity is the mother of invention.” Vannevar Bush¹⁴ distinguished basic from applied research in that the former “is performed without thought of practical ends.” According to Bush, basic research is to contribute to “general knowledge and an understanding of nature and its laws.” Seeing an inevitable conflict between research to increase understanding and research geared toward use, he held that “applied research invariably drives out pure.”

Today, Bush’s “rugged individual approach” has been largely replaced by teamwork. Whether it is a physical paradigm used to apply nanotechnologies to neurological maladies, a chemical paradigm used to find a safe psychotropic drug, or a biological paradigm of disease used to find an effective HIV vaccine, any contemporary paradigm depends on groups of people who are not only technically competent but who are also good at collaborating with one another in order to realize a common objective.¹⁵ Success within this new paradigm requires synergy. This is not the same as acquiescence to a prominent theory. To the contrary, a good team member is one who is willing to point out weaknesses and fallacies in the paradigm.

Basic research is defined by the fact that it seeks to widen the understanding of the phenomena of a scientific field—it is guided by the quest to advance knowledge. Numerous influential works of research are in fact driven by both of these goals. A prime example is the work of Louis Pasteur, who as a basic scientist sought to understand the microbiological processes he discovered, and as an applied scientist sought to use the basic knowledge to address spoilage of vinegar, beer, wine, and milk.¹⁴

The disparity between basic and applied research is captured in the “linear model” of the dynamic form of the postwar paradigm. It is important to keep in mind, though, that in the dynamic flow model, each of the successive stages of development depends upon the stage before it (Example 1). The advancement of science parallels the application of science. For example, does science always lead to engineering, which subsequently drives the need for technology? Of course, this may be the default, but it is not the only transition. Engineering has driven basic science within a paradigm (e.g., bioscience’s “black boxes” that progressively, but never completely, become understood by bioscience researchers). A recent example that should give scientists and engineers pause is “geoengineering.” This is the new field seeks to address global problems with planetary-scale designs. Some geoengineers are already working on ways to address global climate changes. Such actions are commendable if in fact global climate change is anthropogenic. Problematically, some geoengineers have proposed releasing sulfates into the atmosphere because these compounds have been shown to be cooling. However, it is important to remember that the biggest atmospheric concern on the 1980s and 1990s was acid rain, which was largely the result of sulfates and other sulfur compounds that form sulfuric acid when combined with water.

Technology has driven both science and engineering. A new device allows scientists to embark on whole new areas of research (e.g., the microscope dispelled many incorrect germ theories and the polymerase chain reaction has made it possible to advance recombinant DNA research) and engineers to conceive new designs (e.g., the telescope

led the way to space stations and DNA markers allow for enhanced medical and bioremediation projects). However, technology alone does not lead to revolutionary ideas without theoretical advances (e.g., the human genome project was built upon the work of Crick and Watson).

This simple model of scientific advances within a paradigm has come to be called technology *transfer* because it describes the movement from basic science to technology. The first step in this process is basic research within a paradigm, which charts the course for practical application and eliminates dead ends. It also enables the applied scientist and engineer to reach their goal quickly and economically. Then, applied research involves elaboration and the application of the known. Here, scientists and engineers convert the possible into the actual. The final stage in the technological sequence, development, is the stage where scientists systematically adapt research findings into useful materials, devices, systems, methods, processes, etc.¹⁴

The characterization of the processes that lead from basic to applied science has been criticized as being too simple an account of the flow from science to technology. In particular, the *one-way* flow from scientific discovery to technological innovation does not fit with 21st-century science. The supposition that science exists entirely *outside* of technology is absurd in today's way of thinking. In fact, throughout history there has been reverse flow, a flow from technology to the advancement of science within a given paradigm. The innovation of calculus and the inventions of the microscope and telescope, and later examples of fractal dimensions and rDNA illustrate that current science within a paradigm has progressively become more *technology derived or motivated*.¹⁴ The relationship between basic and applied sciences is not universally held. Some agree that: "The terms basic and applied are, in another sense, not opposites. Work directed toward applied goals can be highly fundamental in character in that it has an important impact on the conceptual structure or outlook of an established field."¹⁶

Sound science is actually used to synthesize of the goals within a paradigm. One could argue that Pasteur was among the first to optimize theory and utility. Similar arguments can be made for the historical predecessors DaVinci and Archimedes. The one-dimensional model in Figure 1 consists of a line with "basic research" on one end and "applied research" on the other (as though the two were polar opposites). Pasteur's world view could be force-fit into this model by placing his design paradigms at the cen-



FIGURE 1. Stepwise progression from basic biological research to product/system realization.

ter of the flow in Figure 2. However, Pasteur’s equal and strong commitments to *understanding* the theory (microbiological processes) and to practice (controlling the effects of these processes) would cover the entire line segment. Arguably, two points within a spectrum better represent Pasteur, one at the “basic research” end of the spectrum and another at the “applied research” end of the spectrum. This placement led Stokes to suggest a different model that reconciles the shortcomings of this one-dimensional model.

Research within a university follows a flow similar to that shown in Figure 3, namely, paradigm-driven research. Science departments are concerned with knowledge-building, engineering departments with applied knowledge to understand how to solve society’s problems, and the university designer is interested in finding innovative ways to use this knowledge. For example, the medical doctor at the university’s medical center may know what research has led to a particular medical procedure and the devices used in that procedure, but may want to “figure out” better designs in terms of ease of

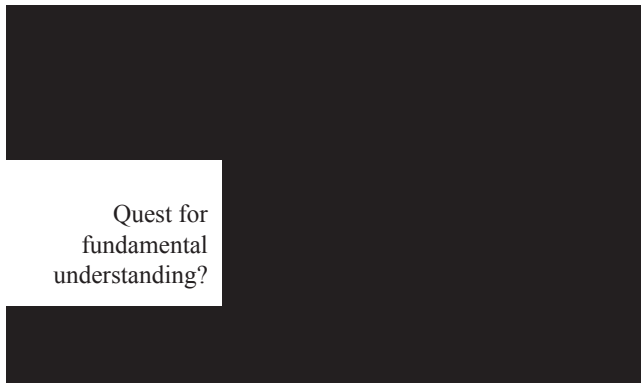


FIGURE 2. Research categorized according to knowledge and utility drivers. (Adapted with permission from Stokes.¹⁴)



FIGURE 3. University biological research categorized according to knowledge and utility drivers.

application, improved recovery time, and better drug delivery. In these cases, the physician is behaving much like Edison, who was most interested in utility and less interested in knowledge for knowledge's sake. In addition, the physician must work closely with the health administrators of the university, who purchase the devices and maintain the systems. This is not to say that innovations do not come from the southwest box in Example 3, because they can. It simply means that the measures of success at the university stress operation and maintenance. In fact, the quadrants must all have feedback loops to one another to support the development of the paradigm.

B. Scientific Advances and Issues

A well-known and documented scientific- and engineering-based event that changed the course of history took place during the 20th century and was an outgrowth of "scientific revolutions": the implementation and completion of the multidisciplinary Manhattan Project during World War II.¹⁷ This highly focused applied science and engineering effort brought together a team from many countries to develop and build the atom bomb as a means for ending WWII. The technological success, though unleashing a highly destructive force to end the Asian theater of WWII, brought the world into the complex era that was named the atomic age and ultimately became an integral part of the "Cold War." The intensity of the efforts to produce the atomic bomb also laid a firm foundation for the design and growth of "big" science programs that are now conducted by multiple laboratories and investigators throughout the world. Some work in collaboration and others in competition for large amounts of resources. During the post-WWII period, three "big" science/engineering efforts were: i) the world starting the race to space and the moon, ii) the start of the nuclear arms race, and iii) the United States starting the war on cancer. Each of these also led to new technologies and products that began to influence other areas of science and engineering throughout the world.

From the discussion above, it is also apparent that the work of science not only influences society, but is greatly influenced by the events and activities within society. Science must be systematic because everything in a system affects every other thing. The "thing" can be a material substance (e.g., a xenobiotic toxin) or an organism (both the agent and the receptor, e.g., a microbe and a human host for a contaminant, or a microbe and ecosystem in a remediation project). The "thing" may also be a process or mechanism. Miller captured this prospective, systematic perspective, adding society's expectation of scientific vigilance: "From stone spearheads to engineered nanotubes, our artifacts can change how we live and, ultimately, who we are. The social significance of technological change requires us to take responsibility for the design, implementation, and deployment of the things we make.... (I)t is clear that technology can change society. But sometimes we lose sight of the idea that society can change technology."¹⁸

Technological changes can arrive at a furious pace, overwhelming scientists and ethicists alike. Either consciously or unconsciously, technological determinism or Chandler's inevitability thesis may become accepted within the scientific community. The idea that technology is going to happen no matter what we do is both tempting and highly

dangerous. We have to keep reminding ourselves that we not only *can* steer technology, but engineers especially must remember that part of their professional responsibility is to shape technology for the benefit of the public at large. More importantly, we need to leave room for truly new discovery, which has becoming increasingly difficult to promote and nurture in the 21st century. .

The post-WWII period saw innovations that led to the introduction of many widely used products and tools into society; including high-speed computers, personal computers, the modern television, advanced waste treatment systems, smart appliances and tools for health care (e.g., magnetic resonance imaging, computed tomography scanning, and transplants) and discovery (e.g., mass spectrometer, chromatographs, plasma spectrometers), rockets, antibiotics, drug therapies, air conditioning, electric lighting of cities and towns, synthetic plastics, transistors, semiconductors, microprocessors, computerized cars and airplanes, and large-scale energy systems (e.g., nuclear power, gas, coal, and oil) needed to run homes and businesses. The “baby boomers” and their children have benefited greatly from the technological advances, but arguably most have had little appreciation of these advances and the efforts of the few who took the risks to make the above and more happen. To some extent, the comforts derived from technology have dampened the desire to seek new discoveries.

C. Science at Risk

The scientific method of the previous three centuries is no longer a universally inviolable construct with which to explain natural phenomena. The metaphorical stool on which science sits is supported by three legs: experimentation, peer review, and publication to allow for replication of results. All three are essential. If any leg is weakened, science risks a nasty fall from soundness to the capriciousness (i.e., from a posteriori to a priori knowledge).

During the second half of the 20th century, many scientific fields became very specialized, forming subdisciplines that led to the introduction of specialized journals and degree programs. In specific cases, many appeared to have been warranted because their content focuses on important data, information needs, or technological advances. Further, many of the issues would not be studied effectively by a field in general. For example, biomedical science appears to be losing sight of general or overarching aspects of each specialty, which by the very nature of expanded opportunities to examine many narrow areas of inquiry could well be deterring the ability of science to examine to paths that may lead to paradigm shifts or possibly a new revolution—losing the forest for the trees, so to speak.

The expanding possibilities for large-scale advances in science and engineering in the post-WWII period anticipated by federal agencies in the United States led to the implementation of the “peer review” grant system, which was designed to systematically stimulate competition for fundamental and applied research. The introduction of grant programs by federal agencies was a logical result of the successes during the early to mid-20th century. However, over time, although still accomplishing many good

things, the systems began to age and preserve the status quo. For example, when submitting applications to many agencies, one cannot propose truly new research in a grant. Preliminary data are needed before the proposal even gets a chance to be reviewed by peer reviewers identified by many federal agencies. In addition, it is not at all uncommon for a scientist to have had a grant reviewed by individuals who have no clue about the topic being proposed to investigate, which of course leads to rejection of a grant by someone with insufficient expertise to determine the value of cutting-edge research. Ultimately, the system can lead to the waste of the many valuable hours required to write and submit the grant and the mountain of required forms, and true creativity is hampered by this process.

To reinforce this point, the average age for an independent investigator to receive his or her first National Institutes of Health (NIH) grant is 42.6 years, and has remained steady at that level since 2002.²⁰ This is not a healthy situation and indicates that the agencies typically have decided to fund what can best be described as “paradigm-fitting science.” Applicants can do little other than to conform to these agencies’ discretion. Even the lay press has questioned this practice related to a 2009 review of cancer research, which observed that although there was good science, and that some poor science was eliminated during review, there was a lack of innovation. The article noted that, “It has become a sort of jobs program, a way to keep research laboratories going year after year with the understanding that the focus will be on small projects unlikely to take significant steps toward curing cancer.”²¹ Such observations lead to the more serious issue of the reasons why projects are continuously re-funded. We seem to learn more and more about less and less. In the final analysis, the constant re-funding of projects may not provide new or major advances after a certain point in time. We believe that a top-to-bottom review is essential.

As an example of the absurdity of the current system, Wilbur and Orville Wright would likely never have been funded for their experiments. They lacked preliminary data showing that flight was not only feasible, but had already been successfully achieved by the investigators. The reviewers, resting on their existing paradigms, might say: “You mean someone thinks they can fly? Reject the application!” In fact, the gatekeepers in the room may get a good chuckle and say some derisive things about the “Wrong Brothers.” True innovation relies on risk taking, and most reviewers of science—scientists—are risk averse. Taxpayers’ money is a precious resource that should go toward the most meaningful and creative ideas; however, this is a very difficult task because science is slow to change even within a paradigm, and today the potential financial gains and losses from such changes can be significant.

The NIH introduced a grant application title called the R-21, which was designed to foster innovation but in the beginning became a miniature version of the regular external grant program. Again, the reviewers did not understand the quest for innovation. The good news is that NIH is rectifying this problem, and has refocused the program on new ideas and actually asks that the innovation be described in the application. We wish them well and success, as it is a move toward their original plan. We would add that the em-

phasis should include funding young scientists. Clearly, today room needs to be made in grant programs to support innovation and the “well-developed hypotheses” of younger investigators. The NIH is also beginning to address this critical need.

The issue of funding creative research is also quite a problem for investigators in new disciplines or, more likely, subdisciplines, because they have a difficult time breaking through the “peer review” glass ceiling. P.J.L. was informed recently by a colleague about a conversation between him and a scientist in which the colleague was trying to make the case for more funding in the innovation field of exposure science.^{22,23} This individual was a member of a more traditional field in environmental health. He was told in no uncertain terms that the field had to stand in line. We are convinced that the time needed to nurture ideas for the next generation of discoveries needs to be embraced by funding agencies. When asked, P.J.L.’s suggestion has been that 15% to 25% of the federal research budget should be devoted to well thought-out but high-risk experiments and analyses.

The situation today for most investigators is a never-ending cycle of grant writing to start a new program or sustain an innovative current program. This cycle starts almost as soon as a young assistant professor or research investigator is hired at a research university from a private company, and it never stops. Although grants are essential to providing information to fill in major gaps in knowledge within today’s paradigms and to improve current technology, the speed at which we try to achieve these goals with funded projects actually decreases our ability to sustain long-term productivity and creativity.

Advances in modern science and technology cost money, and universities and other organizations have a seemingly impossible task in supporting unfunded activities, which makes innovation difficult. More importantly, there are no longer the benefactors and resources available to support long-term innovative research. Even large companies have abandoned their long-term exploratory research programs in favor of short-term research to achieve end-of-the year profits or new products. There are now national laboratories (Oak Ridge, Los Alamos, etc.) that were once part of the Atomic Energy Commission, which dealt with the long-term and complex scientific issues of the Cold War and energy. These have now become similar to academic research institutions, because each competes for some portion of its work with academic institutions that apply for government grants and contracts associated with very specific projects or areas of inquiry. Up until the 1980s, the Bell Laboratories were an icon for the kind of innovative long-term research needed to move science forward in America. Unfortunately, an unintended consequence of the total dismantling of the parent company, Bell Telephone, was the dissolution of the missions of these laboratories, a major loss to society as well as to the scientific world. This was a case in which the legal system was not looking at the long-term consequences of a decision on progress in science. Putting all of the preceding together, one can see that the science and the scientific method have succumbed to the pressures of business and the pace of government intervention in the 21st century. The most immediate question is whether we in the United States abandon the quest to return to the moon and Mars and beyond. It can clearly set a tone for the place of revolutionary

discovery during the rest of this decade. Some would argue that clean or “green” energy is a road to innovation. That may be true, but it is not necessarily discovery. In fact, we already have an important energy source: nuclear power. Unfortunately, it suffers from a lack of rational explanation to the general population of the pros and cons as a source for achieving energy independence.

II. CASES

Although every discipline in science and engineering has numerous examples of the erosion of the scientific method, some particular cases may help to elucidate this drift.

A. The Computer and Internet

Scientists and engineers rely heavily on computers to gather and evaluate data and information and to communicate with individuals around the world. The computer, which evolved quickly for military applications during the Cold War, was a major technological advance, but it is a mixed blessing to society and science. On the positive side for science, business, and technology is its extensive use in the development of high-end computational tools, communications, control systems, and computational models. Computers now allow us to complete detailed analyses of data, to maintain business records and activity, to solve complex and computationally expensive equations, and to solve systems of equations required to answer very difficult problems (e.g., space flight, pharmacokinetics, and process control). Such systems are also valuable in making adjustments to current tools and products that were never before imaginable (e.g., drug discovery and simulation of new designs for consumer and commercial products and systems). High-end computational systems provide for the high-speed transmission of information and the storage of many trillions of megabytes of information. For society, it has expanded the range of advanced, technologically based products in commerce: the Internet for communication and transfer of information, computer games, and other home-based systems and products.

However, within this great expansion of information, technological products, and computational power, there is a negative side that within the current educational landscape can interfere with the ability of science and the application of the scientific method to advance into the future. Basically, we are in information overload. At a fundamental level, the educational programs in science and other fields have changed by virtue of the expansion of available information, yielding a very steep learning curve for new and aspiring students. Thus, the teaching of fundamental concepts is not done to the degree of rigor as it has been in the past; in fact, many rudimentary activities are ignored as students rely on computers and calculators for answers. As a result, the basic level of thinking, reasoning, and exploration necessary to evaluate information and solve problems using the scientific method has been taken away from students. Further, such activities have been taken over by the use of computer programs and applications during the critical stages of intellectual development. As a result, today’s students move through

the academic system relying more and more on computers for all types of analyses and evaluations, and less and less on their own abilities to discriminate the importance of information and draw conclusions. Even in the laboratory sciences, students are conducting virtual laboratory experiments. Does this approach to learning foster curiosity and innovation? The answer is: it is doubtful. It is therefore quite possible that we are producing higher-class technicians who rely on technologically advanced machines to make conclusions at the same time that our educational system is stifling creativity. One must remember that a machine cannot conclude anything beyond the computational power afforded it by the developer. On the positive side, when used properly, computer systems can solve complex problems that it would take centuries to solve by hand.

However, many of us lament the fact that the current generation of students do not go back and check results or the basic reason for selecting a particular mode of analysis or computer program, which can and will lead to erroneous results and probably poor decision making. Smoothing tools and different approaches to averaging can yield fuzzy results and devalue extreme values, which is a critical error. Further, as we obtain more and more accuracy in the values of acquired data, the statistical inferences may be better, but may actually have less meaning because in some cases the numbers themselves are very low and possibly de minimus in value for drawing meaningful conclusions.

B. Value of Information

At the beginning of the second decade of the 21st century, there needs to be a significant retooling of the concept of the “value of information” in addressing scientific problems and other worldly issues (homeland security and business) and the uncertainties that are associated with all information/data. This is imperative because computational tools and power continue to advance. Parallel to this issue, statistical methods currently available to analyze data have been far outstripped by the volumes and types of data that are associated with the variables measured by instrumentation. With the constant streaming of information at a pace of 24/7, it is almost impossible to keep up, but the basic question is, what information/data should be kept and for what purpose? All information is not and should not be valued equally, and archived and well-researched historical information should be valued at a much higher level because it has stood the test of time. Learning how to value information requires retooling of our educational system by returning to questioning and proof of concept before acceptance: the general public’s version of the scientific method. We do not want our children and grandchildren to turn into the “Eloi” portrayed in the Orson Wells novel *Time Machine*. These pathetic creatures were depicted as “people living a life of play and toil less abundance. Then it was revealed that the Morlocks (a sinister tribe from the underground) were attending to the needs of the Eloi’s for the same reason a farmer tends cattle: the Eloi composed most, if not all, of the Morlocks’ diet and no longer had any function beyond this purpose.”²⁴

The optimal societal uses of computational tools are those for which both the computational tools and analytical tools and systems are coupled for efficiency and analysis of information. These are associated with many disciplines; for example, diagnostic

equipment, analytical equipment in chemistry and physics, and applications such as fuel-injection systems for cars, process controls for industries, financial systems, and communications. However, in the case of large-scale data acquisition systems (e.g., microarrays in the area of genomics) the measurement or detection tools themselves have outstripped the abilities of the investigators to use computer-based computational tools to interpret the data, which is technology-driven science. What is amazing is the fact that these very large data sets that include millions of red or orange dots were initially analyzed by the statistical techniques used by psychology, which has very strict data structure rules. Thus, many of the analyses are probably full of large uncertainties but the results could be considered a start for future research and analysis.

A critical challenge is how to develop cost-effective computational tools to analyze these data appropriately in the future for hypothesis generation and testing. For example, the general tools of informatics have been used for many years in engineering, but the current generation of biologists has little or no training to address the complex issue of interpretation of genomics data. This lag between biological science and technology is escalating by the minute because more and more genomics data are being captured and stored each day. The role of mathematics in biology will take on new meaning this century. It is time to start planning now, and successes may lead to the seeds of a new scientific revolution, at least in biology.

To achieve this important transformation in activities, the field of biology must be transformed to include more mathematically orientated activities and tools for hypothesis testing and generation.²⁵ One level of good news is the evolution of a new field called information science; however, this is another subdiscipline that does not necessarily connect directly to other fields in providing the foundation for discerning new discoveries. We fear that information science will be used more for hypothesis generation, which does not point the way to discovering new approaches to scientific inquiry beyond a current paradigm. Science is driven by the intellectual question, not the models and statistical methods available to analyze large sets of data. However, information science should become a part of every science curriculum in the future because it will provide the necessary computational tools for active investigators within each scientific discipline. For society in general, one goal should be to marry the use of information with critical thinking to solve problems. A simple, but not totally realistic example to explain this point is the stories developed and portrayed in the TV program "Numb3rs." Although primarily a TV crime drama, it plants a seed within the viewers that there can be ways to combine mathematics, information, and critical thinking to improve our society through a better understanding of the "value of information."

A further challenge for the survival of scientific method is the proliferation of information on the Internet that has not been and probably will never be subjected to review. Until the late 1990s, the main source of scientific information was journals associated with one or more particular areas of research and the presentation of preliminary and final results at scientific meetings. With social networking, thoughts are streamed throughout the world. In spite of the opportunities for recording information and com-

munication, such systems in can instantaneously spread premature and potentially erroneous information, which can spawn partially developed or unproven theories taken to be the truth. To the uninformed these can be easily packaged as truth on the Internet, and can and will lead to many levels of misinformation and in some cases scientific fraud. Add to this the very entertaining “reality” TV programs, and we will have to work hard to differentiate showmanship from the truth. We have no real answer to these problems, and we doubt that anyone does; however, it appears that scientists must be willing to attack the fraudulent claims one at a time to try to ensure the integrity of each field and to find review mechanisms that can employ the Internet as a way to recapture the truth. In the late 1980s there was the example of “cold fusion.” The apparent discovery was published in the peer-reviewed scientific literature.²⁶ The findings were then tested and found to be non-reproducible. This apparently was not a deliberate “fraud,” it was just a poorly validated experiment. The process of peer review and experimental redundancies and replication, however, worked and eventually the idea was sent back to the laboratory. The system of checks and balances in science worked well in that case.

In contrast, the global warming issue has evolved from an area of scientific inquiry to an almost “cult-like” issue since it was revealed that there had been a systematic effort by a number of scientists in the global climate change community to squash alternate opinions, to promote biased explanations of data, and even to modify raw data. The peer-reviewed literature and major reports are replete with projections, anecdotal observations, and speculations, not a norm for scientific literature. However, many of the reports appear to be devoid of a thorough presentation and review and discussion of the *uncertainties* in data and the models that attempt to the relationship between carbon dioxide and temperature—the touted relationship—in the scientific literature.^{5,27} The movie “An Inconvenient Truth,” is not a proper way to present science. One would be excused in thinking so given its popularity with science teachers (not to mention environmental science, philosophy, and religion professors, as well as Academy Awards and Nobel Prize committees). Indeed, the scientific community must build a truly independent and honest process of peer review and interpretation of all climate data and results to re-establish trust in the process and to build trust in future conclusions. Both what is known and what is unknown should be boldly proclaimed by scientists. When describing biomedical and environmental phenomena, there is always uncertainty, so scientists must embrace humility and avoid hubris. We must be honest about what we do not know. This must occur without regard to any social or political position. Such objectivity must be inculcated, as affirmed by Einstein: “Whoever is careless with the truth in small matters cannot be trusted with important matters.”²⁸

Expanding access to the Internet coupled with activism, pressure is increasingly applied for science to fit to policy rather than policy being driven by sound science. Thus, science must reclaim its position of neutrality in discovering the truth. Unlike law, science cannot rely on the preponderance of evidence. One experiment can begin a paradigm shift; otherwise, we would have science by plebiscite. We would simply vote on issues like a congress or appoint a science czar who will tell us what is true and our

paradigms would respond in kind. To some extent, this may well already be happening. An Associated Press poll asked the opinion of a small group of scientists regarding the propriety of selective handling information in the so-called Climategate scandal. The majority of respondents perceived no fraud.²⁹ Could this be because each of us has a unique definition of “fraud,” or is it that those scientists polled do believe that the ends are justified by unscrupulous or at least very sloppy and “convenient” means? Perhaps a follow-up question would have been useful, such as, “even if there are no data to support the conclusion that the globe is warming, would you still believe the globe is warming?” We are in trouble if even a few scientists answer “yes.” Indeed, the seriousness and potential ramifications (e.g., ecological, health, economic) of human-induced climate change demands a sound scientific underpinning.

C. Endangered Species

A few years ago, scientists debated whether to stick with existing taxonomic classifications of the black and green sea turtles. For decades, biologists had believed that there were two distinct species, the green (*Chelonia mydas*) and the black (*Chelonia agassizii*) turtle. However, with advances in DNA and other techniques to characterize genetic relationships, it was becoming obvious that the turtles were actually so close genetically that they are in fact the same species. Such debates often go beyond academics and often raise important policy questions. In this case the question is whether protection under the Endangered Species Act (ESA) should continue to be extended to the not-so-abundant black form of the more abundant green sea turtle. The truly scientifically derived information based on DNA strongly indicates that the black sea turtle should not be considered an evolutionarily distinguishable species from the green sea turtle and the only distinction is that of a “geopolitical species,” one made without regard to “morphological, genetic and reproductive criteria.”³³ The scientific method would seem to have ended this debate among scientists, but it did not. The debate raged on, with scientists asking some pretty scary questions: Should the black sea turtle be re-classified as a color morph of the green sea turtle, possibly jeopardizing its protections under the ESA? Should the ESA guidelines for what to protect be modified to extend protection to identifiable subpopulations in cases such as this, where there is no geographic or genetic evidence that they are evolutionarily distinct from the main population? Where should the line be drawn for species and subspecies on the scale of genetic distinctiveness and is this open to some debate? Should scientists interested in conserving the black form exploit that uncertainty in order to press for continued protection of the black turtles?

The journal *Conservation Biology* decided to put these questions before its readership by publishing a series of articles containing scientific, philosophical, and ethical perspectives on how science should be used in relation to the goal of turtle conservation.³³⁻³⁷ Many scientists agreed that the new genetic information was trustworthy, but worried that it would lead to some unintended and negative consequences for turtle conservation. Some writers called for a “geopolitical taxonomy,” where the black sea turtle would continue to be considered a distinct species even though the genetic in-

formation made that view difficult to justify. The analogy of war was invoked as a justification, with one writer declaring that “it is acceptable to tell lies to deceive the enemy.” The debate moderators asked a telling question: “Should legitimate scientific results then be withheld, modified, or ‘spun’ to serve conservation goals?” Continuing with the war analogy, some scientists likened the deceptive taxonomy to propaganda needed to prevent advances by the enemy.³⁸ That is, the disinformation and “spin” would be justified by some noble end: protecting the turtle under existing law! This prompts some important questions:

1. Is there a greater good at stake here that supersedes the usual standards of sound science?
2. Is it scientifically legitimate for the proponents of a social goal such as turtle conservation to exploit scientific uncertainty in service of that goal? To withhold or distort scientific information?
3. Conservation biology has been described as a “crisis discipline” because it is focused on an urgent and practical end, conservation of biodiversity. Does this create an inherent conflict for conservation biologists?
4. Can scientists play both technical and advocacy roles in an ethical way?
5. How could this sort of controversy be handled?
6. What general lessons about the responsibilities of scientists in society might be derived from this case?

Some scientists have sympathized with a climatologist and former government advisor who argued that scientists ought to “offer up scary scenarios, make simplified dramatic statements, and make little mention of any doubts we may have. Each of us has to decide what the right balance is between being effective and being honest.”³⁹

Such a distorted version of “utilitarian science” is destructive, violating the first canon of science: honest inquiry and reporting.⁵ Not every scientist buys this. Such debates expose the acceptance by some to justify the use of morally unacceptable means to achieve the greater good.⁴⁰ Misinformation is a weapon, they seem to argue, and weapons are morally neutral. Only the application and intent of the weapon determines the morality. The problem is that, as Snow would put it, once one ceases to tell only the truth, *all* credibility of one’s research is lost, and such is the case even for a seemingly noble cause.³⁷ Shrader-Frechette and McCoy emphasize that credible science requires that “...in virtually all cases in professional ethics, the public has the right to know the truth when human or environmental welfare is at issue.”^{34,37}

Ends justifying means is common in many venues. For example, politicians recently proclaimed that they do not want “waste a good crisis.” That is, a devastating hurricane or record high summer temperatures may offer unique opportunities to take public actions that would not normally be acceptable to the majority. A potential outbreak of swine flu may give public health officials a platform from which to support other, unrelated

health policies. Such is politics and not science. The scientific community may need to wait to report scientifically sound information, even if that means the crisis is “wasted.” When scientists begin to sound like politicians, it is time to assess the role of advocacy in our conclusions. We should worry that we are losing objectivity and, as a result, our credibility. The public often paints with a broad brush, so even meticulous and careful science may be difficult to distinguish from “junk science.”

Perhaps the most troubling part of this debate is that it occurred at all. Once we start treating the truth as a commodity, who can blame the public for losing confidence in science and its practitioners? Certainly, not C.P. Snow.

III. BIAS IN THE CONDUCT OF RESEARCH

An overt problem has evolved over with the past 40 years and places stress on the scientific method. It is what we call, “activism-based hypothesis testing.” This concept has significantly infiltrated science and the funding of areas and subareas of scientific research. Researchers have accepted federal and other funds to study an area of inquiry that has been mandated by a group with vested interest in the outcome. Within our fields, these include issues related to the environmental causes of specific diseases, environmental justice, and species loss in the environment.

First, we must put some boundaries on the above statements because there are many legitimate scientific questions and problems that are generated by the issues of the day, and are identified by the public, not scientists. Within this group is the important issue of environmental justice, which is manifested by a lack of or lax cleanup or poor urban planning in areas with populations at high risk for disease.³⁰ However, we do have to be wary of the fact that in contrast to the basic premise of the scientific method that we prove or disprove hypotheses, activist-based hypothesis testing on one side or another of an issue seeks in information primarily to prove a point. The rejection of the hypothesis may well be unacceptable to an activist. Consider the controversy about the role of vaccines in causing autism. This hypothesis was advanced in a *Lancet* article published in 1998.³¹ It was not until 2010 that the fraud was finally acknowledged and the original article was withdrawn.³² How many children needlessly suffered from the debilitating effects caused by measles over the past 12 years? In the end, objective peer review highlights errors.

Disagreements about scientific methodologies can be genuine. In the turtle case, surely not every scientist disagreeing with the single species designation based his or her position on advocacy. They may well have been opposed based on the credibility of the science underpinning the arguments. This goes on constantly in scientific research. Scientific skepticism must be encouraged. In fact, the Federal Research Misconduct Policy explicitly states that research misconduct “does not include difference of opinion.”³⁷

Conflict of interest, however, is not always direct. It is bemusing when some investigators who obtain resources from the federal government and other agencies say that they have no conflicts of interest or biases, especially when their work is a response to a specific request for data or results by a company or government agency. An even more

indirect but profound conflict involves the finding of negative results for a hypothesis. No matter the quality and importance of such an investigation, additional funding is doubtful, as is the likelihood of publication in the scientific literature. As reviewers for many major journals we find it remarkable that a well-designed and well-conducted negative study in the environmental health sciences is not usually treated with the same level of enthusiasm as a positive finding. In addition, sometimes the authors of submitted manuscripts are reluctant to say that the results were truly negative: a pity, but true. However, we do commend efforts by those who find negative results in persisting to publish those results. It would be nice to have as a lead story someday the following “study shows that dimethyl XXX does not cause disease YYY. We believe that sort of honesty does resonate with the public. In contrast, we get headlines about a cure or some major breakthrough in science when in fact the investigators have solved some small problem in the totality of issues associated with a problem.

A corollary conflict is the dearth of interest in replication of investigations to ensure that the findings are correct and are being interpreted properly. A recent example had to do with the synergistic effects of pesticides.⁴¹ An important study by a respected research group found that hormonal effects are multiplied when an organism is exposed to more than one of these pesticides simultaneously. Such a finding is crucial because if true, the allowable levels of exposure should be dramatically less than if the effects were additive. However, the publication was withdrawn because subsequent studies could not replicate the results. The good news is that not only the original investigators, but others attempted to replicate the results. A commentary in *Environmental Health Perspectives* put it this way: “While these actions have been very painful for all involved, they are an essential part of the process that makes science a unique human enterprise. In science, the fallibility of human involvement is minimized over time by observing and re-observing, testing and retesting. Data that do not support the consensual reality of science are replaced or quickly forgotten.”⁴²

While this is the intent of credible science, there is really little incentive to replicate others’ work. It is likely that relatively little “re-observing, testing and retesting” is taking place, especially when such revisiting involves so-called “settled science.” Thus, the scientific community is likely to be slow to respond to erroneous data, and this is exacerbated with the fact that consensual reality is influenced by factors other than science.

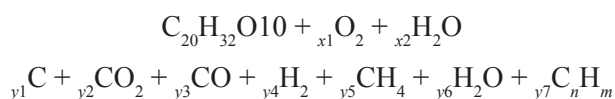
Boyle’s three requirements of science, experimentation, publication, and peer review, have been amazingly durable through the centuries. All three are essential and interdependent. Without a posteriori evidence to support it, a hypothesis is mere conjecture. Without peer review, publications can say just about anything. Without publication, there is no way for the scientific community to evaluate the soundness and integrity of findings. Thus, when journals do not encourage replication of results, they invite problems in all three requirements.

Scientists must also be particularly careful about subscribing to a particular ideology. The current raging debate regarding the measures of safety of products is instructive. On its face, this appears to be a straightforward decision: simply choose the approach that

will lead to the safest outcome. Historically, the United States has subscribed principally to the view that one needs evidence of risks and from this evidence makes a decision. Others (e.g., many European regulators) would like to approach safety from a precautionary view. That is, if the potential consequences of this decision are irreversible, long-lived, or otherwise dire, then the decision should be to avoid that product. Who wouldn't choose the latter approach?

Actually, many *do* oppose such a precaution for at least two very basic reasons. First, a purely precautionary mentality is anti-science at the extreme. The cynic might say that it encourages us to be blissful in our ignorance. If the same metrics were applied to most scientific programs, such as the Space Race, fundamentals of matter, and yes, even finding cures for cancer and AIDS, major parts of these programs would not have even been started let alone completed. The preceding statements points to the second major problem with the precautionary principle when taken to the extreme: it does not allow evidence of benefits and risks to be evaluated together. We could be preventing a problem but losing an even more important opportunity. For example, the risk of emerging fields such as nanotechnology certainly come with risks, but are very likely to produce untold benefits (e.g., drug-delivery systems that may allow for the treatment of heretofore untreatable cancers).

Blind precaution does not respect that everything in science is part of a system. Every component of that system affects and is affected by every other component of the system. It takes the reductionist view to every challenge and to every problem. As an example, first-year undergraduates at Duke University recently were asked to consider a very basic reaction in which an organic compound is oxidized in the presence of water and heat. In fact, this reaction applies to most thermal processes (i.e., gasification, pyrolysis, hydrolysis, and combustion):



Note that the reaction has both complete combustion products (carbon dioxide and water) and incomplete combustion products (carbon monoxide, elemental carbon, hydrogen, methane, and various organic compounds). Guess which compounds the class worried about almost unanimously? No, it was not the very toxic carbon monoxide and the many organics that include carcinogens and other hazardous compounds. They were the most worried about the carbon dioxide and methane. Thus, to extend this to its ridiculous conclusion (reduction ad absurdum), the precautionary approach would be to avoid anything that emits either of these compounds (which is basically every living thing on earth). The point is not to argue whether these two compounds are radiant gases: of course they are. The problem with an exclusively reductionist view is that picks and chooses the things that are important without regard to their relationships to all of the other things in that system

Open and honest debate is the lifeblood of science. Nearly everything should be up for debate by scientists. The subject matter of a debate varies widely among disciplines,

but any scientist must be entitled to ask questions and, yes, even to debate areas even outside of his or her primary area of expertise. In fact, some of the best scientific questions are those brought from another field, such as microbiologists who brought new views on wastewater treatment to civil engineering, chemists who helped biologists map DNA, and physicists who saw new ways to approach medicines.

The bottom line is the continuing need to couple science and truth, and the truth depends on openly sharing facts—even inconvenient ones. From these facts, hypotheses can be tested. If the facts and findings support the hypothesis, we still need to know how certain we are about what the test is telling us. We may find that our hypothesis was limited because the facts upon which it was based were conveniently supportive of a preconceived notion. That is not science!

IV. ISSUES THAT AFFECT THE USE OF THE SCIENTIFIC METHOD

Society relies on the Internet for almost all of its information. It is inevitable that with the availability of the Internet to students, good and bad habits and outcomes are possible. Users have access to volumes of information that we never had in our youth, which is of great value in finding information on many topics. The problem is that the information is not necessarily vetted prior to use, which requires an assessment by the potential user after each click to a Web site. The other problem is that even correct information may be aggregated in ways that detract from knowledge. Data simply exist. Facts simply exist. At a workshop of the National Academy of Engineering, scientists were warned that they are entitled to opinions but not to the facts.³⁷ Researchers certainly must debate the data's meanings and give appropriate attention to their various interpretations, but we must not redefine facts simply to fit our paradigms. We may not like what the facts are telling us, but we must be objective if we are to follow the scientific method.

Data and facts do not become information until they are manipulated by users and the scientific basis of the data is repeated by others to achieve coherence.⁴ Further, such information does not become knowledge without being integrated meaningfully by those who understand their context. Unfortunately, anyone can "Google" a key word and gather mounds of data, even those who have no idea what such data mean. There is an excellent commercial that has been running in which people are asked a simple question, but answer in highly technical yet irrelevant ways (e.g., in response to a question of what's for dinner, they may respond that the Irish hen eats only green potato caterpillars during an Aurora Borealis in odd number leap centuries). Rather than information overload, this is information nonsense. Even worse, data and facts can be manipulated to become misinformation and fraud.

Obviously, the lack of assessment can lead to the use of misinformation and fraudulent or doctored information in an analysis or examination of an issue or use of information. Again, our educational system has not caught up with how to handle the volumes of information and how to effectively discriminate real versus false concepts and theories. Information has always been available, but never to the degree that it is currently accessible to young minds. In the past, P.J.L. made it mandatory that students

not use the Internet for information gathering. D.A.V. has always allowed it, but never counts anything being with “http” or “www” as a scholarly citation. However, we both understand that today it is no longer a cause worth fighting because reputable scientific journals now publish online. However, the need for accurate references and the need to discriminate between open access journals with and without peer review is essential if science is to grow and yield new discoveries. Students can spend their life surfing but not end up with the perfect wave.

Far too many students and others are being seduced into thinking that if it is not on the Internet it is not worth reading. This leads to a big problem for science: the notion that science began in the 1990s needs to be addressed in attempting to educate the next generation. Because students will use the Internet extensively, to prevent reduced accessibility to scientific information, journals must seriously consider scanning historical volumes to online portals, as is being done with more and more books. This will reduce the probability that individuals will try to re-invent well-known successes and failures in science and engineering. Clearly, we need to make sure the documented history of individual scientific disciplines is not lost. The body of work should also be placed into the context of the major achievements (value of information) and principles that established the science, the practice of each science over time, and the uncertainties and questions that remain today. With such a foundation, students will have a better appreciation of the past and a firm foundation so that new discoveries will have a better opportunity to evolve. Part of the goal, however, should not be to have a taxonomy particular to one scientific field, but to provide a basis for re-establishing the need for critical thinking and fostering creative analysis. In the end this is a necessary theorem for productive communication, debate, discovery, and progress.

With the continuing addition of new information and academic courses within many disciplines, there has been increasing degradation of personal or individual inquiry. Universities and other levels of education are forgoing the basics and making up courses for non-science majors designed to pick a multidisciplinary topic and present snippets from a variety of disciplines to explain specific points and major concepts. It is very disconcerting that individuals are being steered in this direction. Again, the basics are being lost, as is the ability for the student to discriminate the truth, especially when only one side of the issue is taught or the alternate explanation is not given serious consideration.

A corollary to this problem is found in the first phase of any good scientific endeavor: the literature review. Perhaps to please granting agencies or simply to show the currency of a research project, most cited works have been conducted in the past decade. A colleague recently indicated that very few researchers look for relevant research that took place over 20 years ago. This invites “re-inventing the wheel” and wasted resources going after previously discovered information. Further, to paraphrase George Santayana, by our ignoring scientific lessons of the past, we are likely to repeat our mistakes.

As we have seen with the issue of global climate change, there are biases on both sides of a scientific issue. However, the recent revelations from Climategate suggest that society in general must seriously reassess its views on scientific claims that appear to be driven

by political or other agendas. As stated earlier, this type of struggle has existed in the past, but the speed at which society and science are transferring all types of information and personal opinions make the future of allowing good science to prevail difficult to achieve and sustain without thoroughly evaluating all sides of the science freely. A major mistake can lead to unnecessary and even counterproductive expenditures of resources.

Climategate has also reminded us about the scientist's "value added." Much of what we provide is interpretation. Most often, data are incomplete, so we must either interpolate between data points or extrapolate from data points to interpret meaning. Interpolations and extrapolations may be mathematical, scientific, or subjective. Mathematically, the extrapolation can be made from the region (or range) of observation to the region of extrapolation. For example, there may be points observed from epidemiological studies. The extrapolation is often used as weight of evidence, such as whether a chemical agent causes cancer. A much greater tumor effect from chemical X versus chemical Z could result from errors in study design, measurement, or other experimental flaws, or it could be that the study differs from the others (e.g., different means of dosing the animals such as oral versus dermal, different organs tested, or the presence of a "promoter" in the diet or elsewhere). Either way, scientific extrapolation will have to determine why these studies differ. These points are interpolated to generate a curve in the region of observation, but there are no actual results from experiments available below these dosages. A number of statistical methods can be used to extend the curve to the origin. This is all part of the uncertainties scientists must address. However, sometimes scientists believe so strongly that the data "must" support a hypothesis that they focus on a pre-ordained answer! This is not only unscientific, it violates the tenets of what Sigma Xi has called "Honor in Science."⁴³

Certainly, some data have to be discarded. Scientists must be able to distinguish when data may and should be ignored, when are outliers important, and what they may tell us that other data do not. We often remind our students, however, that the outliers are where Nobel Prizes are won in science or, at a minimum, solutions are found to problems. The problem is when advocacy trumps scientific integrity and the appropriate use of scientific findings, especially the temptations and pitfall of "trimming, cooking, and forging" data to support a certain hypothesis.⁴⁴ Any data that are not used must be clearly noted, along with the rationale (e.g., a statistical modeling technique) for their omission or selective use. In other words, Boyle's requirement for peer review ("witness") depends on complete transparency.

Mathematics has been called the language of science and it provides a means for communication among the disciplines. As a primary example, biologists must be able to understand and use mathematics in their testing and proving of hypotheses, or at least have enough mathematical training to guide the analysis of large data sets by those trained in informatics. The amount and complexity of biomedical, environmental, and other data obviates the possibility of simple explanations and statistical analyses for discovery in the life sciences.

V. CONCLUSIONS

The scientific method remains the benchmark for the conduct of credible research. Today, research is being affected by the interests and the activism of government agencies, public entities, and others. Therefore, in the United States at least, research priorities can be altered substantially every two to eight years, which does not bode well for true innovation and discovery. This problem will not easily or quickly change, but the continuity of scientific discovery requires research that adheres to the scientific method.

Students need to be educated at all levels on both the basic principles of science and how to properly employ new tools and computational systems to explore data. The means of achieving this can begin with a meaningful national dialogue on the role and use of science in our world.

Scientists must be vigilant to ensure adherence to the scientific method because objectivity is essential for true innovation, as has been demonstrated since the 17th century. As was the case then, researchers must be prepared to be criticized for being “overly” careful about their observations, data quality, approaches to test hypotheses, and ways to ensure that research is reproducible.

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Community Engagement in Observational Human Exposure Studies

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ABSTRACT: Although observational human exposure studies do not deliberately expose participants to chemicals or environmental conditions, merely involving people as research participants and conducting research inside homes raises ethical issues. Community engagement offers a promising strategy for managing these ethical concerns by ensuring that the community has a voice in the research process. Community engagement ensures that the research aims, study design, and dissemination activities are relevant to the concerns of the community. One approach is to include qualified community members on the research staff as consultants for protocol development and contributors to the data collection and interpretation processes. A second approach is to seek community consultation, creating dialogue to incorporate the experiential knowledge of the residents. Community advisory boards can serve as a liaison between participants and researchers. Lastly, use of community-based participatory research methodologies actively involves the community in each step of the research process, but requires greater willingness to share decision making. Several issues will affect the collaboration: identification of the community, development of trust, awareness of cultural differences, power and infrastructure differentials, and stakeholder interaction. Researchers must remember that ethical action during all phases of research is necessary for maintaining productive relationships with communities.

KEY WORDS: human exposure; observational studies; community engagement; participatory research; community consultation; research ethics

I. INTRODUCTION

Observational human exposure studies are conducted to understand the extent to which people come into contact with chemicals and other environmental stressors in their everyday lives. These studies involve the collection of environmental and biological samples and questionnaire information from study participants as they go about their normal activities. Although they do not deliberately expose participants to chemicals or environmental conditions, these studies do involve people as research participants, which raises ethical issues.¹ Including children as participants, in particular, raises a range of potential ethical concerns including those related to informed consent, financial incentives, parents' perception of risk, and the duties of researchers to child subjects and their parents.²⁻⁴ One promising strategy for addressing and managing many of these ethical concerns is increased community

engagement through community consultation and participation in the design and implementation of the studies.^{4,5}

Community engagement promotes active community involvement in the processes that shape research strategies and the conduct of research studies. Involvement of community partners ensures that the study design, methods, and dissemination activities meet the diverse needs of the participants and that the research aims are relevant to the concerns of the community. Furthermore, the community's knowledge of the locality, culture, and history can lead to improved research strategies that are sensitive to community values and perceptions. Community engagement takes on even greater importance in observational exposure studies in which researchers typically request that participants provide biomarker samples (e.g., urine, blood, etc.), detailed activity logs, and access to homes for screening and monitoring of chemical constituents. Observational exposure research places a great burden on participants to provide data to support the study objectives, so the active participation of community groups and leaders is crucial to successful participant recruitment and retention efforts and appropriate dissemination of the results that will promote healthy behavior changes.

The document *Ethical Considerations for Research on Housing-Related Health Hazards Involving Children*³ points out that researchers working in the homes and communities of the participants face issues different from those working in a clinical setting. It emphasizes that bidirectional communication between researchers and the community is critical to the scientific and ethical foundation of a research study in such a setting. The article presented here examines opportunities for community engagement in observational research. It details how the involvement of the community can improve the research effort scientifically and ensure that the effort is conducted under the highest ethical standards. Approaches to engaging communities in research are reviewed, important aspects of the community-researcher relationship are identified, and strategies for maintaining the relationship are discussed.

II. DEFINING "COMMUNITY"

"Community" refers to a group of people united by a shared attribute, and the attributes can be wide-ranging, such as geography, culture, social characteristics, values, interests, traditions, or experiences. For observational field studies, the preferred definition of community is the population from which study participants are selected. This definition excludes individuals from government agencies, industry, and others who do not necessarily represent the interests of the participants.⁶ Central to the definition of a community is a sense of inclusion and exclusion from membership. A person may be a member of a community by choice, as with voluntary associations, or by virtue of their innate personal characteristics, such as age, gender, race, or ethnicity.³ As a result, individuals may belong to multiple communities at any one time. Understanding and describing a community involves exploring factors related to people (including socioeconomics and demographics, health status, and cultural and ethnic characteristics), location (geographic boundaries), commonalities (including shared values, interests, and motivating forces),

and power relationships (including formal and informal lines of authority and influence, stakeholder relationships, and resource flows).⁵ When initiating community engagement efforts, one should be aware of these complex associations in deciding which individuals to work with in the targeted community.

It is important to distinguish between stakeholders and the community, but both should be engaged at some point in the course of a study. Stakeholders are groups or organizations that may affect, be affected by, or perceive themselves to be affected by a decision or activity. Stakeholders may have a direct or indirect interest in the “matter” of interest. They may include individuals; environmental, social, or community nongovernment organizations (NGOs); government entities; businesses; and industry. A critical difference between the community and stakeholders is that stakeholders cannot represent or speak for the community. Although relationships with stakeholders can be confrontational, stakeholders often provide useful information and expertise. When the stakeholder and community member roles overlap in particular individuals, it is important to distinguish the role in which the individual is acting.⁶

Quandt et al. discuss a research project, “Preventing Agricultural Chemical Exposure in North Carolina Farmworkers,” in which the process of defining a community was complicated by language, ethnic and racial stereotypes, and lack of organization.⁷ Many of the affected farmworkers originated outside the United States from several different Spanish-speaking countries and possessed contradicting viewpoints on research and the utility of community organization. Moreover, the community organization tailored for this farmworker demographic did not include enough members to adequately populate the study. The researchers utilized multiple approaches, including community forums, community advisory councils, and public presentations, to identify a diverse yet viable community within the broader farmworker population. Through this process of using multiple participatory strategies to define the community, a sense of community was nurtured among the farmworkers collectively.⁸

III. APPROACHES TO COMMUNITY INVOLVEMENT

True community engagement, as used in community-based participatory research (CBPR), requires the active involvement of community partners in each step of the research process. This includes decisions about study design, study methods, dissemination of findings, and resulting actions. Even when observational exposure studies are not CBPR studies, there is an increasing demand by communities for a greater role in the scientific research and decision-making processes that impact their lives.⁹ Researchers are under increasing pressure to abandon the traditional “decide-announce-defend” paradigm in favor of more extensively utilizing community knowledge in both defining and addressing important research issues. Rather than restricting community engagement to the implementation phase strictly for recruitment purposes, the goal should be to incorporate community knowledge into the entire research process as early as during the initial framing of the issue. Regardless of the extent to which the community is involved, researchers should adhere to the nine basic governing principles outlined by the Centers

for Disease Control and Prevention (CDC) for engaging communities in health-related research (Table 1).⁵

Table 1 Community Engagement Principles for Researchers

Requirement	Explanation
Clarity	Clear communication of the study objectives, research goals, and the populations or communities of interest
Knowledge of the Community	Familiarity with the economic conditions, political structures, demographics, history, past research experiences, and research perceptions of the community
Visibility	Travel to the community, interact with formal and informal leadership, and establish relationships to build trust
Acceptance	Acknowledge, without judging, the assets and deficits of the community
Partnership	Balanced discussion and shared decision making among participants concerning risks, responsibilities, expectations, benefits, and investment
Respect	Value the diversity of culture, history, beliefs, and opinions within the community for improved understanding
Asset Utilization	Identify and mobilize community assets to improve scientific credibility of the interpretation and dissemination of results
Flexibility	Anticipate changes within the community in regard to perceived benefits of research and stakeholder interest and additional time and resource needs
Commitment	Prepare to engage the community beyond the constraints of the research projects, before and after, to promote longevity of the relationship for future research

From the Centers for Disease Control and Prevention.⁵

A simple form of community involvement is to include qualified members of the community on the research staff. Paid research staff members from the community can serve as valuable consultants for protocol development and research design, including how to collect the data, how to recruit and retain participants, and how to interpret and disseminate the results. However, including paid research staff from the community may introduce a conflict of interest among community members: community representatives may feel a greater allegiance to the researchers providing the payment and be less inclined to uphold the interests of the community. In addition, the community may come to view the paid research staff from the community as “outsiders.” To help to alleviate these potential issues, researchers should ensure an equitable distribution of paid research work among different groups within the larger community so as not to promote a perceived bias among community members. Additionally, when possible, researchers should make efforts to provide payments to community members employed as research staff through community partner organizations to prevent conflict-of-interest issues.

Two recent Environmental Protection Agency (EPA)-involved studies, the Detroit Exposure and Aerosol Research Study (DEARS) and the Environmental Risk and Im-

pact in Communities of Color (ERICC) study, included community members as paid members of the research team.^{11,12} In the DEARS study, the community researchers were instrumental in recruiting study participants from the seven study neighborhoods in Detroit, Michigan. The success of DEARS was dependent on researchers developing strong relations with community leaders and state and local organizations. The ERICC study employed a community liaison who had lived in the community for several decades, was well known to local residents in minority and non-minority groups, and worked at one of the industries included in the study. The liaison not only facilitated communication among the residents, representatives of local industries, and the scientists conducting the study, but also assisted with organizing the study and sample collection and contributed to the successful completion of the study.¹⁴

A second approach to community involvement is to seek community consultation and review. Researchers may periodically meet with community residents in a process of “engagement, dialogue, and feedback” to discuss research plans, research progress, and results.¹⁵ The objective is to seek a dialogue with community residents to promote co-learning and asset sharing between the researchers and the community. Open, honest, jargon-free communication is imperative to the success of this approach. Effective communication ensures that the community has a voice in the research process. Having a voice increases trust and engagement in the research, which in turn makes the research more applicable to the community’s needs. Authentic community consultation embraces the “experiential knowledge of the average citizen.”¹⁶ When developing research budgets and timescales, researchers who plan to incorporate community consultation and review in the research process should take into account the additional expenses and time necessary for community marketing efforts and travel.

Corburn describes successful community participation in an EPA exposure assessment in Brooklyn, New York.¹⁰ He explains how a shift of focus from risk assessment to exposure assessment may provide an opportunity for community engagement to improve the technical assessment. Listed among the specific factors integral to the assessment’s success was the incorporation of local, non-expert information during the consultation and review process, which was used to modify the conventional risk-assessment process. Another factor was the inclusion of community-based organizations on the scientific research team as contributors to the data collection, modeling, and interpretation processes, where they provided data and expertise not available through traditional research frameworks.¹⁰

Community advisory boards (CABs) also have been used as an approach for getting the community involved in research efforts.¹⁷ A CAB could be formed to serve as a liaison between participants and researchers. In particular, CABs can advise the researchers about community concerns and assist in the development of materials to explain the study to potential participants. CABs should be sufficiently large to ensure a diversity of community views, perspectives, and attitudes. Representatives from the board may be selected for participation on the research team and could function as an oversight committee in case of any participant grievances. According to Quinn, the success of CABs “lies in the ability of the researchers and CABs to form a true partnership, enabling their

different voices to be heard equally.”¹⁷ Unless the researchers are truly open to working with the CAB, however, the CAB may be perceived as “window dressing” and harm relationships with the community.

O’Fallon and Dearry describe how the Tribal Efforts Against Lead (TEAL) partnership collaborated with the EPA to clean up and minimize exposure to toxins from a Superfund site in Ottawa County, Oklahoma.⁸ The TEAL project utilized the services of a CAB that included representatives from several local tribes to ensure that the research would be responsive to the needs and concerns of the tribal residents. The CAB facilitated researcher interactions with target communities “by helping the investigators interpret data and distribute information to the communities” and “developing and conducting the training” of the community members on risk reduction strategies. The value of the research to TEAL target communities would have been diminished had a CAB not been formed to assist researchers with specific best practices when engaging tribal members and the appropriate tribal leadership structures.

Another potential approach to involving the community is to use a CBPR approach wherein the community is actively involved in each step of the research process, including sharing of decision-making power and resources. This affects decisions about study design and methods, dissemination of findings, and resulting actions. Information about CBPR approaches can be found online at: <http://www.ahrq.gov/clinic/epcsums/cbprsum.htm>. Israel et al. reviewed the results of CBPR efforts at six children’s centers co-funded by the EPA and the National Institute of Environmental Health Sciences¹⁸ and found that considerable commitment of resources and time is needed for the approach to be successful, and that translation of research findings into interventions and policies is of utmost importance. Community partners played little role in defining the research topics and data analysis, but were vital to disseminating the findings to the community. Keeler et al. describe using CBPR methods to evaluate personal and community-level exposures to particulate matter among asthmatic children in Detroit.¹⁹ The research partnership, Community Action Against Asthma (CAAA), consisted of representatives from local health organizations, community environmental advocacy groups, state and local governmental agencies, and academia. The CAAA partnership credits community involvement as active research partners in the research process with the success of the project to acquire “more relevant exposure data for the study of children in urban neighborhoods” and to provide “immediate knowledge and understanding of the outcomes and results of the combined environmental health analysis to the communities.”¹⁹

There are, however, several limitations to utilizing CBPR methods that researchers should consider before developing a CBPR project. The CBPR process is time-consuming, because it takes time to develop partnerships, establish and agree on research aims and objectives, disseminate results to the community using appropriate methods, and review manuscripts and presentations. For this reason, this approach is not conducive to situations in which rapid decisions are necessary given a tight timeline. Weighing the research need versus the community’s desire for researcher intervention is the greatest source of tension in conducting CBPR studies.²⁰

One additional opportunity for community input may involve participation on an institutional review board (IRB). IRBs are required by the Common Rule to have members who are sensitive to “community attitudes” [40 CFR 26.107(a)] and researchers have no influence on how they meet this obligation. A number of recent articles about IRBs, however, have identified a need for more regulatory reform.²¹ Ideally, the IRB should take into account the views of the community. Quinn recommends a greater role for CABs.¹⁷ She argues that there are “ethical issues related to research with communities that are distinctly different from the ethical issues related to research with individuals.” Gilbert goes even further. He suggests supplementing or even replacing traditional IRBs with environmental health and community review boards (EHCRBs).²² He argues that traditional IRBs are inadequate for the review of community-based research because they were developed to address issues related to individuals involved in research projects, not communities. He proposes EHCRBs that combine the fundamental and ethical concept of traditional IRBs with an expanded ethical construct of dignity, veracity, sustainability, and justice, with added emphasis on community. He envisions that an EHCRB would function as an IRB with the requirements and responsibilities that review the protection of human subjects, plus the additional role of reviewing community issues associated with the research project. Gilbert’s recommendation for EHCRBs is consistent with National Research Council (NRC) recommendations that “institutional review boards that review housing health hazards research involving children should ensure that those boards have the necessary expertise to conduct a complete and adequate review, including expertise on research involving children and community perspectives.”²³

Involving community representatives in the IRB process is challenging. One challenge is providing sufficient training to community members about the IRB process and IRB governing regulations. This can be significant if members sit on an IRB for a limited time to review specific community-based studies. In some cases, IRBs may invite community members to participate in the IRB process as non-voting members to solicit the community perspective. This approach, which would be completely at the discretion of the IRB, might reduce the burden on the community representative by reducing training requirements.

IV. IDENTIFYING WHO REPRESENTS THE COMMUNITY

To sufficiently represent the community, an individual should have not only the right to speak for the community’s interests (a right afforded by legitimate membership in the group) but also the ability to describe those interests. Identifying those who represent the community is not simply a matter of identifying the most vocal activists because those individuals do not necessarily represent the interests of the entire community. In fact, several individuals may be necessary to adequately represent the diversity of viewpoints within a community, and in such cases a CAB may be appropriate.⁶ One of the researcher’s first steps should be asking the potential participants from the community who they see as a legitimate representative, someone who can speak for them. Corburn cites an example of an area in Brooklyn, New York that contained individuals with widely dif-

ferent backgrounds.⁹ It was impossible to identify appropriate spokespeople, or even to define the nature of the community, without talking with community members.⁹

The NRC addresses the issue of who should represent the community. Some communities may have a formal governmental structure and a recognized political authority (e.g., Native-American tribes).³ Other communities may have clearly identifiable leaders (e.g., religious communities), whereas still other communities have no formal leadership structure at all. Whether there is a legitimate political authority or some other hierarchal leadership structure, the goal is to seek community input about who best represents the interests of the community with regard to the proposed research project, rather than selecting those who are favorable to the research project. The NRC report cautions against the ethically questionable practice of seeking out population spokespeople and research participants whose positive response to a research plan can be predicted in advance and refers the reader to an article on this topic by Juengst.^{3,23}

With multiple sources of leadership and authority in many communities, careful consideration should be given to what aspect of the community a particular person will represent, and what efforts may be needed to ensure that the entire range of views in a community are obtained. Researchers should consider reaching out to multiple organizations such as churches, social service agencies, community-based organizations, and tenant and other community advocacy groups.

V. BUILDING RELATIONSHIPS AND TRUST

A key first step in developing trust is to establish a relationship with the community before the study. A long history of research with no direct benefits and no feedback of results to the community, however, can contribute to a general mistrust of researchers by community members.²⁴ Moreover, the recurring abuse of trust in communities is a reality that researchers should be aware of when attempting to build a long-term relationship.²⁵ Past ethical failures have created distrust among some communities and have produced great challenges for current community organizers. Although it may seem self-evident, researchers need to remember that ethical action, during all phases of the research, is necessary for developing and maintaining the trust of communities.^{5,26}

Developing trust is a difficult and time-consuming process. Israel et al. suggest a number of ways that community and research partners can gain each other's trust.²⁰ First, partners can *show respect* by seriously considering the ideas and opinions of others. Second, trustworthiness can be demonstrated by *following through* with those things that each partner commits to. Third, partners have to *respect confidentiality*. Fourth, they recommend *attending to each other's interests and needs* by participating in activities beyond the specific work of the partnership. A history of prior positive working relationships is also beneficial.²⁴

Trust cannot be separated from respect. Potential participants need to see researchers fostering respect for community members and leaders to gain trust. For example, meeting with key community leaders and groups in their surroundings helps to build trust for a true partnership. Such meetings provide organizers of engagement activities with more infor-

mation about the community, its concerns, and factors that will facilitate and constrain participation. Once a successful rapport is established, the meetings and exchanges with community members can become an ongoing and substantive partnership.⁶

One mechanism for helping to build trust may be to develop a contractual agreement with the community. A community contract outlines the roles and expectations of both the researcher and the community. Living up to these agreements builds trust with all partners, and the establishment of the agreement helps to reduce misunderstandings. Contracts or memoranda of understanding that outline the roles and expectations of the researcher and the community are discussed in both Israel et al. and Minkler and Wallerstein.^{20,25} An example outlining expectations in a partnership with tribal communities is presented in Appendix E of Minkler and Wallerstein,²⁵ and an example discussing access to data and authorship issues is presented in Appendix I of Israel et al.²⁰ An example of a memorandum of understanding between the University of Michigan School of Public Health, Detroit's Working for Environmental Justice, the Detroit Hispanic Development Corporation, and the Warren Conner Development Coalition for a study investigating asthma is available from: http://depts.washington.edu/ccph/pdf_files/MOU10.pdf.

Work within communities involves a considerable investment of time by researchers and residents. It should be an ongoing, interactive exchange of information and ideas between researchers and community members in which voices are both heard and honored. Trust is fostered when all interested parties feel that they have influence and that their input contributes to the community effort. The collaborations should be inclusive of the entire community, including those members with incompatible interests and perceptions. If participation, influence, and benefits are limited only to some of the partners, then distrust is likely and potential benefits of community involvement may be lost. Being inclusive can create some organizing challenges, but the benefit of effective community involvement "has the potential to lead to greater understanding of community perspectives of the risk and benefits of research, improve informed consent, increase study enrollment, enhance data validity and quality, and build trust for research."³

VI. IMPORTANCE OF LANGUAGE AND CULTURE

Even when all partners and community members are speaking the same language, some terms are not necessarily understood by all. Communications with participants should be reviewed by all partners to ensure that the language used will be appropriate for all participants. At times, one method to communicate research findings will not fit all community members and partners. Even among the partners, understanding each other's meanings is essential so that all partners can move forward with a common understanding.²⁰

Furthermore, Minkler and Wallerstein note that "research must be produced, interpreted, and disseminated to community members in clear, useful, and respectful language."²⁵ Researchers, and especially researchers in a government agency, may have their own distinct lexicon. Researchers should be careful to avoid acronyms, jargon, or technical terms that may obscure the meaning or intimidate participants who are not familiar with the terms. Communicating in "plain language" will help to

build a strong relationship with the community and the participants and also help to enhance trust.²⁷

Culturally sensitive communication is necessary to developing effective research partnerships with communities. To develop effective communications, researchers must understand key aspects of the cultures influencing the intended audience and then build that understanding into the communication strategy.²⁸ The symbols, metaphors, visuals (including clothing, jewelry, and hairstyles), types of actors, language, and music used in communication materials all convey culture. Discussions with community members can assist researchers in identifying messages and images that resonate across groups or suggesting situations in which different messages or images are likely to work best.

Building and maintaining appropriate community and stakeholder relationships requires acknowledgment of the diversity within communities with regard to many factors, including, but not limited to, race/ethnicity, religious beliefs, heritage, and lifestyles. Different groups in the study area may have different cultural norms and practices. The researchers should take these issues into consideration as they work in the community. Community partners can help researchers design the study to be attentive to the increasing heterogeneity of community groups and to the different boundaries of privacy (crucial when designing sampling strategies) of different groups.^{20,25}

Vega provides a thorough discussion of the theoretical and pragmatic implications of cultural diversity for community research.²⁹ He explains that researcher methods for interacting with communities should promote understanding and demonstrate sensitivity and competence in working with diverse cultures (e.g., with respect to class, gender, ethnicity, race, age, and sexual orientation). To aid in this process, researchers should include sufficient time in their project timeline to interact and dialogue with the community before the study begins to understand the cultural issues that may affect the research. Researchers and the results of their work are expected to promote a strengthening of the community; however, it should be recognized that, given the heterogeneity and the diverse views within a community, the study findings potentially may conflict with the desires of the community or may promote feelings of anger or distrust among members of the community. Enlisting the services of a third-party evaluator/mediator may be useful for sustaining positive relations between all research participants and the community at large.

The Research Triangle Park Particulate Matter Panel Study, an EPA investigation of particulate matter and related pollutants involving African-Americans in North Carolina, demonstrated an effective strategy for using communication to address cultural differences between the community and research personnel.¹³ Before beginning the research, the study design included time and finances for building collaborations with organizations having close ties with the African-American community to establish trust between the community and research team. Using input from the community partner organizations, the researchers developed a systematic communication plan to establish rapport with the community and to guide interaction between study participants and the key study personnel. A well-designed and culturally sensitive communication plan was

integral to the success of the study. Eighty percent of the original participants completed the four-season study.¹³

VII. BUILDING A LASTING INFRASTRUCTURE

Infrastructure is anything that builds the capacity of the community by providing members with skills and resources.⁶ When involving the community in the planning process, investigators need to be forthright about funding limitations and research expectations, such as publication and dissemination of results. The community needs to be made aware of the ephemeral nature of funding, even if it results in apprehension toward involvement.

Researchers should communicate early in the process issues that will become important once the research has been completed, such as sustainability. Frankness is required to cultivate community confidence and expertise over time. Because so much time and investment is involved in building an appropriate relationship with the community, researchers may wish to continue their relationship with the community after the study has ended. Researchers should remain accessible for technical support related to the subject of the research. Helping community members to identify new funding opportunities and assisting with the writing of grant applications are two examples of potential continued relationships. Many private sponsoring institutions already recognize the importance of enduring commitment and have used a variety of approaches, often involving funding, to ensure that these relationships are able to continue.⁶ The challenge will be for universities and federal agencies to be able to establish similar funding mechanisms.

The objective of capacity building is to involve members of the community in certain roles (e.g., performing interventions) by training them to perform some of the functions initially performed by the research team. Certain research grants specifically support this type of training. Training can be reciprocal; allowing the community to train the researchers (e.g., in cultural sensitivity) not only fosters respect but also can lead to important new understanding.

Another important step is to formalize the relationship between the community and the institution conducting or sponsoring the research, not just between the community and the individual researcher. Institutional relationships can survive even if individual researchers leave. Institutions may be reluctant to build enduring relationships with communities if they do not see long-term financial value in this investment. Researchers may be able to get more support from their institutions if they can document their successes.⁶

VIII. IDENTIFYING AND INTERACTING WITH OTHER STAKEHOLDERS

Like community involvement, stakeholder involvement in a research study can take many forms. Also like community involvement, researchers should engage stakeholders in their studies early in the planning stages. Relationships between researchers and the various stakeholders should be maintained during the study. How this relationship is maintained can be expected to vary with different stakeholders and may change as the study progresses. Stakeholders can provide useful information

and perspectives during the planning and implementation of observational human exposure studies. If the stakeholders express an interest in participating, the research team should develop a plan for interacting with them that includes roles and responsibilities, activities, and timelines that are mutually agreeable to the team, community representatives, and the stakeholders. Failure to have clear agreements may lead to misunderstandings about the roles of the stakeholders. When developing relationships with stakeholders, researchers should also ensure that participation of the stakeholder in the study, regardless of level of participation, does not result in actual or perceived conflicts of interest. This should be addressed in the plan and agreement for stakeholder involvement.⁶

Stakeholders may include individuals, NGOs, businesses, industry, and various government entities or agencies with jurisdiction over or interest in the community. Stakeholders are a separate entity apart from the community, although they may conduct business or operate within the community or have a direct or indirect interest in community activities. Even though they are not able to speak for the community, stakeholders may have knowledge of impacts and ideas about how to interpret and use the results of proposed research studies. Such knowledge may prove very helpful as part of the research planning and scoping.⁶ Including a variety of stakeholders in the planning process provides insight that comes from reconciling the disparate perspectives of different stakeholders.

Examples of NGOs that may be stakeholders include the Natural Resources Defense Council, Environmental Defense, American Lung Association, American Academy of Pediatrics, American Chemistry Council, and literally hundreds of other organizations with interests in environmental or public health issues. Researchers should identify potential stakeholders and communicate with them early in the planning stages of a study if they are determined to be appropriate. Identifying the appropriate stakeholders who have a legitimate interest in the study will be done on a study-by-study basis and should be done in consultation with the research team, the community representatives, and senior management.

The concept of “stakeholder” has been discussed in management literature since the 1980s. Mitchell et al. have developed an approach for identifying the relevant stakeholders through an assessment of their power, legitimacy, and urgency.³⁰ Such an approach may be useful for identifying stakeholders to be involved in the research studies. In describing CBPR, Israel et al. discuss the need to examine the advantages and disadvantages of extending membership beyond the “community of identity” at the outset.²⁰ For example, they discuss the relative merits of including representatives of the agricultural industry in a study of farmworkers because of industry’s possible role in policy change, and weigh their inclusion against the concerns that the true voice of the farmworkers may not be heard under such conditions. They also describe a possible solution of creating separate partnership groups. O’Fallon and Deary explain the benefits of including diverse stakeholders for the dissemination of results.⁸

IX. CONCLUSION

Community engagement is needed in exposure research to ensure that the rights and concerns of the individuals are respected, that research protocols are well-implemented and address community concerns in a fair manner, and that interpretation and dissemination of findings include community input. Involving the community in the research effort can improve the research both scientifically and ethically. There are multiple approaches to engaging communities in research: through community consultation and review, as paid research staff, as members on community advisory boards, and by involvement in community-based participatory research. Each of these approaches comes with a set of benefits and limitations that researchers should consider when discussing a potential project. Because relationships in and with communities are dynamic, methods and strategies used to interact with the community may evolve over the course of the study. There are a host of other issues to consider when engaging communities in research that will affect the collaboration; these include identification of the community, development of relationships within and trust with the community, awareness of language and culture differences, power and infrastructure differentials, and interaction with stakeholders. Because abuse of trust and other ethical failures have created distrust, researchers must remember that ethical action during all phases of the research is necessary for developing and maintaining productive long-term relationships with communities.

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- ▶ Animal testing for medical devices
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- ▶ Ethics of genetic engineering and cloning
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Conference Chair

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SUNY Downstate Medical Center

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New York University

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Polytechnic Institute of NYU

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