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INTRODUCTION

The genesis of the topic of bioscience-business ethics is the realization that DNA knowledge can be applied to produce breakthrough medical, agricultural, and other products. Just over 50 years ago, James Watson and Francis Crick unraveled the structure of DNA; 2 decades later, the first two biotechnology companies, Cetus and Genentech, were founded. Since then, there have been great advances in biotechnology: in the 1980s, the first biotech drugs reached the market, and in the1990s, the first genetically engineered crops became commercially available. These new industries and products are beginning to have a dramatic impact on human health and agriculture. We are now well into a biotechnology revolution that has transformed both the ability to generate medical and agricultural products and the industries that produce these products.

Physics dominated the first half of the 20th century; the 21st century has already been dubbed the *age of biology*.[1] The sequencing of the genomes of the major crop plants, many animals, pathogens, and humans has laid the groundwork for a new, genetically driven approach to medicine, agriculture, nutrition, and many other fields. Biotechnology has so invaded the methodologies of the traditional medical, industrial, and agricultural companies that, as an industry, they collectively deserve a new name—what we are calling the bioscience industry. There are still relatively few major biotechnology drugs on the market, but the number of new biological drugs in clinical trials now exceeds the number of novel, small molecule, chemical-based drugs in development. And despite the European controversy surrounding their introduction, biotechnology crops (now called *genetically modified*, or *GM*, crops) are growing at a rapid rate, already accounting for a majority of the soybeans and cotton grown in the United States, with global sales projected to reach $25 billion by 2010. The potential impact of new biotechnologies

[1]Shahi G. *BioBusiness in Asia*. London: Prentice Hall; 2004.

extends well beyond health and agriculture to a variety of other industrial and environmental implications that may account for up to 50% of the gross domestic product (GDP) of world economies by 2050.[2]

There is another reason to group and rename the industry that is producing these new biotechnology products. Their very nature raises such profound social and ethical issues that managers in these companies now have to address concerns emanating from the relatively new field of bioethics, as well as the older field of medical ethics. Looking back, there were hints that this phenomenon was coming. In the 20th century, public concerns about safety and misuse caused major setbacks in the development of nuclear power and recombinant DNA technology that presaged similar attacks against genetically modified crops. Applying lessons from these three examples makes it plausible to predict that public concerns about issues such as cloning, stem cell research, genetic privacy, human genetic enhancement, and antibioterrorism technology can pose a greater risk to the future of the bioscience industry than the technologic challenges themselves.

Given this potential risk, some bioscience company managers have begun to address the social and ethical consequences of producing biotechnology products. These efforts are driven in part by an interest in protecting companies from harm. But other motivations also are at play, driven by the realization that the role of corporations in the use of biotechnology products is so vital that failure to address ethical concerns risks stalling scientific advances and wasting the potential for building a healthier society. Companies at the forefront of incorporating biomedical ethics into product development decision making are plowing new ground; there is, as yet, no well-established body of scholarship to guide them. This book, based on a research project involving in-depth case studies of 13 bioscience firms, aims to begin to close this gap.

ETHICAL ISSUES CONFRONTING BIOSCIENCE COMPANIES

The ethical issues facing bioscience companies are likely to vary based on their particular technology, product focus and stage of development. Some examples of ethical issues that firms are facing as they progress from research to bringing products to market include:

- Who owns genetic information? Is it socially equitable and feasible for commercial firms to own genetic information? Does this unfairly inhibit academic research? How do firms respond to those who claim that no one should patent and sell human genetic information? What consent, if any, do firms using this information need from individuals and communities?
- Is it responsible to develop and market genetic tests for conditions for which there is as yet no related prevention or treatment? Who bears responsibility for those individuals who lose medical insurance or employment when, using a company-developed gene test, they are identified as possessing disease-related genes?
- How should pharmaceutical and biotech firms price their drugs and other medical products in a global economy, to ensure that they can justify the major research costs and risks, and still provide the maximum access and benefit to those in need in both the developed and developing countries?
- What constitutes fair and balanced medical product marketing to physicians and the public? Do the benefits of direct-to-consumer advertising outweigh the corporate and social costs?
- How does a company manage the inherent conflicts of interest in its funding of the clinical trials of a medical product that it intends to market? At what stage should it be obliged to disclose publicly the results of its research, including negative findings?
- What are the economic, social, and health implications of the move toward more personalized medicine? (Targeting treatments much more specifically to individual underlying genetic conditions improves health outcomes but reduces the target population group, and hence the potential market, for drug development firms.) Will individuals and societies be able to afford it?
- How can the benefits of genomics and biotechnology be extended to billions of people in developing countries, in an effort to avoid creating a "genomics divide" between industrialized and developing countries?

The rest of this introductory chapter is in four sections.

1. We examine why bioscience firms should address these ethics questions. By using the term *bioscience business ethics,* we intend to include the ethical issues that attach to:
   - the technologies that these companies commercialize (medical, agricultural, etc.)
   - the manner in which these technologies are researched in animals and humans
   - the way that drugs and other products are marketed and sold

   Depending on the phase of product development, a bioscience business manager is likely to encounter ethical issues in all these areas.
2. We describe the development of the field of biomedical ethics, placing its interaction with bioscience firms in an historical context, and addressing some of the associated controversies.
3. We describe the methods used in the research that led to this book. We interviewed more than 100 senior decision makers to develop the 13 case studies from which we have attempted to derive lessons for the development of bioscience business ethics.
4. Finally, we provide an overview of the rest of the book, to explain the logic of how we grouped the company case studies. The cases can be read individually; however, we encourage readers to read this overview chapter first.

[2]Ibid.

The concluding chapter pulls together lessons learned from the cases on how bioscience companies approach those aspects of their business that raise ethical issues.

WHY SHOULD BIOSCIENCE FIRMS CARE ABOUT ETHICS?

Although this work is a study of how companies are managing bioscience ethical issues, there are reasons why many have not adopted this managerial practice. To provide a broad understanding about the current state of affairs on our subject, we examine the most common arguments from new bioscience firms against the need for dealing with ethical issues. We follow with our counter-arguments about why it is prudent for bioscience firms to overcome the objections and address the ethical issues raised by the products they develop proactively.

Argument No. 1: *We're worried about raising enough capital to survive and to see if our technology works; we don't have the time or money to worry about ethics.*

Bioscience is one of the riskiest bets an investor can make. Of every 10 companies they back, venture capitalists generally expect only 1 to become a major success, hope that 2 or 3 others will yield some return on investment, and assume the rest will fail. To make money, given bioscience's inherent uncertainties, these investors and the companies they fund must become experts at managing many types of risk: technical, financial, regulatory, and managerial. They screen hundreds of business plans, weeding out any with risks considered unacceptably high. The last thing they want is to add additional risk—regarding either a bioethics or business ethics issue—that could undermine the future of the company. The near-impossibility of obtaining any funding in today's market for a business model that involves GM foods is an example of this unacceptable risk. This is not because of concerns about the feasibility of the technology nor the size of the potential market. It is because of the global controversy surrounding the initial applications of GM crops, which has made the prospects for regulatory and consumer acceptance of any next-generation product highly uncertain. Harsher critics would say that, as ethical issues are now known to be an inherent aspect of commercially developing biomedical technology, firms that do not plan for ethical analysis are guilty of a failure of vision. So it would pay an early-stage bioscience firm seeking to raise capital to anticipate ethical concerns and develop responses to them.

Argument No. 2: *We're too small. We'll worry about ethics when we get a product to market.*

Given that it typically takes a decade or more to go from laboratory research to getting a new drug on the market, it is not surprising that many bioscience start-ups do not feel a sense of urgency about addressing ethical concerns. Many argue that, because the failure rate is so high (only a small percentage of initial

compounds make it through the clinical research phase), it is a waste of time and effort to focus on ethics at the early stage of drug discovery.

Our research and that of others suggests that bioscience companies miss important opportunities when they assume that they will need to address ethical issues only after a mature product has been developed. As the Genzyme, Millennium, Novo Nordisk, and Affymetrix cases in this volume reveal, the culture and values established in a company's early days by founders and leadership teams have a profound and lasting effect on the subsequent ethical decision making of the organization, even decades later when the company has evolved into a large global business. To cite an analogy that has become a general rule of organizational change, it is easier to change the course of a small speedboat than a supertanker. Likewise, it is far more difficult to change an organization's culture and approach to ethical issues at a later stage than to instill the ethical values and priorities from the outset. This is also true in the more narrow sense of individual products. Identifying at the outset which ethical issues are likely to attach to a particular product informs all subsequent decisions about that product and prevents getting blindsided by unanticipated reactions.

A solid foundation in ethical decision making will enable companies to see, at each stage in product development, where the minefields may lie. For instance, there are always business, technological, and medical aspects to the first decision most companies make—that is, what products to develop. Adding an ethical dimension to the decision can generate useful insight, such as when companies decide to forego short-term profits from an expensive "me-too" drug with only marginal benefits over existing drugs, and to execute instead a business plan to produce a first-in-class drug to fulfill an unmet medical need. Many would argue that society needs the latter and not the former. The company, however, may not be able to afford the socially responsible choice. An ethical analysis would force the company to consider the utility, the consequences, and the justice of each potentially feasible option. Whatever the decision, the company proceeds with an understanding of the potential ethical objections to that choice and how those objections can be mitigated. Assuming that most business choices in this industry have an ethical dimension allows managers to see and manage the ethical aspect of all activities, such as animal and human research, contracting with academic physicians, data publication, pricing, advertising, off-label use, or post-market monitoring, all of which have produced ethical problems for companies, with the consequent negative press and financial costs. Companies founded on a coherent set of values and an ability to incorporate ethics into decision making find it much easier to see where the ethical issues lie and how to address them.

Argument No. 3: *We're fine so long as we follow FDA guidelines.*

The Food and Drug Administration (FDA) and its counterparts around the world play such a powerful role in regulating the bioscience industry that it is not surprising many managers in these companies feel they are behaving ethically as long as they comply with what the FDA requires. But, as a general proposition, legal compliance alone never ensures that companies are shielded from allegations

of unethical behavior. There are two specific difficulties associated with conflating FDA compliance and ethics. First, what the FDA requires changes often and, especially for cutting-edge technologies, it may be years before it supplies clear guidelines on how companies should proceed. For example, the FDA never required the producers of GM foods to demonstrate human safety, just equivalency to natural foods. Many herbal medicines are marketed with little, if any, FDA oversight. Genetic tests, if marketed as testing services, can be sold with no safety or efficacy data submitted to the FDA.[3] The FDA is almost inevitably at a disadvantage compared with the knowledge possessed by company experts working on a new technology. Hence, regulatory evolution often trails the evolution of technology. This is clear in several of our case studies of pharmacogenomics or nutrigenomics firms that seek to link drugs or foods to an individual's genotype. The FDA has not yet developed a full set of guidelines to govern how these products get to market. In the absence of regulation, having an ethical justification for key development and marketing decisions can only benefit, as it is more likely that the agency will approve what the company has done and might even adopt the ethical reasoning of the company to generate an industry standard. The Monsanto, Interleukin, and Sciona cases illustrate the ethical problems that can occur when developing technologies in a regulatory vacuum.

Relying solely on the FDA to determine the right actions to take creates a second, related problem for companies, which is what the FDA demands is not always considered ethical. This is most clearly brought out in the Genzyme case: the firm argued vociferously (but ultimately in vain) with the FDA over the design of a Phase IV clinical trial because it believed it would be unethical to ask doctors to continue to give some patients a placebo when the drug was now approved for sale and no other viable treatment alternatives were available.

Argument No. 4: *We are ethical. Our whole business is about helping people.*

Corporate scientists and managers may be fully convinced that the research they are doing, and the products they are developing, will be beneficial for mankind. However, it does not follow that all or even a majority of the public will agree. The leaders of Myriad Pharmaceuticals thought they were helping women when they marketed the tests for the breast cancer *BRCA* gene. However, the company encountered strong opposition from breast cancer activists who thought that the gene test was harmful because it resulted in women being told they carried a breast cancer gene, but there was nothing reliable they could do to prevent the disease. Companies also have been labeled "unethical" when they deny access to clinical trials to desperately sick patients who do not meet the research entry criteria.[4] A number of the cases in this volume demonstrate that interest groups and nongovernmental organizations (NGOs) can oppose the marketing of bioscience company innovations, no matter how beneficial the company believes the product to be. For instance, Monsanto scientists went from being convinced that

[3]Eaton ML. *Ethics and the Business of Bioscience.* Stanford, Calif: Stanford University Press; 2004.
[4]Eaton, 2004.

the GM crops they were creating could reduce environmental pollution and help feed needy populations in developing countries to being reluctant to identify themselves as Monsanto employees because of the opposition their firm faced. Likewise, Diversa Corporation expected public approval when it voluntarily decided to exceed the stipulations of the Convention on Biological Diversity for sharing the benefits stemming from its research. Nevertheless, Diversa has encountered opposition for seeking to profit from nature's genetic diversity.

Although the human health applications of bioscience research have generally been more favorably received, a number of issues remain, such as the use of animals in research, applications of embryonic stem cells, handling of genetic information, access to medicines once they are developed, which can cause significant problems for bioscience companies. To anticipate any issues that may arise, to shape policies and educational activities that may alleviate criticism, and to build awareness of the potential benefits of their activities, it is useful for companies to analyze the ethical context of their decisions long before their products reach the market.

In addition to the arguments above, our research and earlier works[5] have identified a number of other reasons why bioscience firms should bring an ethical perspective to their business decision making. Unquestionably, the most common reason we heard was, "It's the right thing to do." Managers saying this not only highlighted the strong normative dimension of taking an ethical approach to business, but also told us that there were some tangible business benefits, including:

- helping to attract, motivate, and retain some of the most talented scientists and other employees
- enhancing the image of individual companies and an industry that, at least in the case of bioagriculture and pharmaceuticals, has fallen in public trust
- making it easier to attract strong, high-quality business partners
- attracting the growing number of socially conscious investors who are factoring corporate and social responsibility (CSR) into their evaluation of companies
- reducing the likelihood of the very large legal settlements and personal criminal liabilities that some bioscience companies and their executives have faced for such things as overly aggressive patent protection, misleading data interpretation, poorly managed drug toxicities, deceptive marketing practices, or inducements to prescribe
- Finally, in an industry that is wholly dependent on the government for approval of its products and much of its revenue, adopting a strong approach to self-regulation as part of good governance practices may be the best means to avoid greater restrictions imposed by government on their license to operate.

[5]Dhanda RK. *Guiding Icarus: Merging Bioethics with Corporate Interests.* New York: Wiley-Liss; 2002; Eaton, 2004.

ETHICISTS AND THE BIOSCIENCE INDUSTRY

The previous section addressed why bioscience companies should care about ethics. This section addresses how biomedical ethics has evolved along with the bioscience industry. We document three approaches.

In the early days of the bioscience industry, there was a long period of distance and skepticism between bioethicists and the corporate world. During this time, most academic ethics experts, (along with interest groups and the media) criticized the industry from the outside, and there was relatively little direct interaction between the ethicists and the industry. More recently, some bioethics experts have moved to the other end of the spectrum, going to work for bioscience companies, either as consultants or employees, to help them deal with the complex ethical issues companies face. In our study, we suggest a third way: conducting detailed research *in,* but not *for,* bioscience companies, to try to improve our understanding of the ethical decision making process in the corporations that are pushing forward the bioscience revolution.

Bioethics and biomedical ethics have their roots in medical ethics, which has existed as a moral guide to the practice of medicine since antiquity. A particularly strong resurgence in medical ethics took place after the Nuremberg Trials revealed the atrocities committed by Nazi physicians in their experimentation on prisoners of war. The resulting Nuremberg Code of Ethics in Medical Research (1946–1949) sparked a movement in medical research ethics. Stimulated again by postwar revelations of research misconduct, such as the infamous Tuskegee Study,[6] another expansion in ethics concern resulted in the development of the national and international guidelines, regulations, and laws that set new standards for what is considered ethical conduct in human research.

Additional concern about the activity of medical scientists resulted in a new term, *biomedical ethics,* which started appearing after the consumer and protest movements of the 1960s. Amid the general questioning of power, the professions of medicine and science did not escape scrutiny for the ways medical treatments and technologies were used. Physicians were denounced for ethical failures, such as when "God committees" used social-worth criteria to decide which patients had access to scarce dialysis treatment. Scientists were condemned when it was discovered that they had exposed unwitting people to nuclear radiation. How to avoid the abusive application of new medical and related technologies became such a widespread concern that it led to the formation of several government commissions. (The President's Commission for the Study of Ethical Challenges in Medicine and Biomedical and Behavioral Research, and the Advisory Committee on Human Radiation Experiments, both sponsored by the United States government, are two examples.) Products of this era were bioethics centers (such as The Hastings Center), the introduction of ethics teaching in medical schools, and the formation of hospital clinical ethics committees that sought to ensure ethical treatment of patients.

[6]When a group of African American men were infected with syphilis without their knowledge as part of a medical experiment.

Soon thereafter, scientists recognized the need to engage in public debates on the ethical implications of new biotechnologies. A notable example is the 1975 Asilomar Conference, convened by the Nobel Laureate biochemist Dr. Paul Berg, where scientists involved with new recombinant DNA research agreed voluntarily to halt their research until the safety concerns about the technology had been addressed and resolved.[7] The lessons of Asilomar, however, did not penetrate deeply. In the 1980s and 1990s, new technologies (in vitro fertilization, embryonic stem cells, genetic testing, etc.) continued to spark debates about whether they were being used before their full impact on patients, medicine, and society was fully understood.[8]

The ethics climate changed drastically when, in 1988, the Human Genome Project (HGP) became the first large scientific undertaking to dedicate a significant portion of its research budget to associated ethical issues and created HUGO (the Human Genome Organization). HUGO's purpose was to foster international collaboration and provide study guidance for international ethics and intellectual property issues linked to the decoding of the genome. In the United States, the Department of Energy devoted 3 to 5% of its HGP budget to a program that would conduct prospective and concurrent research into the ethical, legal, and social implications (ELSI) of genome research.[9] Other funding agencies, such as Genome Canada, have built on the lessons, both positive and negative, of the HGP's ELSI program to devote an even larger percentage of their funding to large-scale bioethics programs. These lessons also are being incorporated into similar European Union initiatives and the United States National Nanotechnology Initiative. The ethics initiatives associated with the HGP set the important precedent that scientists must now address the ethical issues associated with their work as part of seeking funding for their research.

The need for these ethics initiatives was clearly demonstrated as the genetic advances that accompanied the HGP attracted growing public concern. This ethical concern then began to include industry: when companies such as Incyte and Celera began to seek patent rights for human genetic material, critics claimed that corporate ownership would limit the access of non-profit and academic researchers to valuable genetic tools. Some argued that no human genetic material should be owned by anyone, least of all a for-profit corporation, and thus challenged the very existence of bioscience companies.[10]

The new ethical challenges that accompanied innovations by bioscience companies were occurring against a backdrop of ethical issues that had existed for decades within the pharmaceutical industry. For reasons often related to the cost

[7]Reconsidering Asilomar. *The Scientist.* 2000;14:15. Available at http://www.the-scientist.com/yr2000/apr/russo_p15_000403.html.

[8]See, Rose H, Rose S. (2003, July 3). Playing God: Eggs from Foetuses, Artificial Wombs, Dead Men's Sperm—It's Not Only the Religious Right Who Object to Such 'Advances.' *The Guardian,* p. 25.

[9]Collins FS, Morgan M, Patrinos A. The Human Genome Project: Lessons from Large-Scale Biology. *Science.* 2003:300:286–290.

[10]Waldholz M, Stout H. (1992, April 17). A New Debate Rages over the Patenting of Gene Discoveries. *The Wall Street Journal,* Section B1.

and safety of prescription drugs, pharmaceutical companies and their device and vaccine cousins have been under more or less constant criticism from academia and the media since the consumer movement started in the 1960s. Groups that lobby against these companies are AIDS activists (ACT-UP was formed specifically to protest the price of the first anti-AIDS drug); breast-cancer advocacy groups that protest the denial of access to experimental cancer drugs; religious groups against companies that use embryos in research, or that market contraceptive- or abortion-related products; environmental activists against companies that market genetically modified foods and crops; and animal rights groups whose attacks against firms and their employees who use animals in scientific research have sometimes escalated from verbal abuse to physical violence. These anti-industry groups began to form alliances and to demonstrate at the annual Biotechnology Industry Organization (BIO) conferences to get their message across that biotechnology companies could not be trusted and would remain under scrutiny.[11]

The steady stream of allegations of corporate misconduct against a few high-profile companies bolstered the general perception that bioscience companies place profits before the welfare of the patients who use their products: media revelations of companies taking shortcuts with research protections, rigging trials, hiding negative research results, paying for scientific opinions, providing kickbacks to physicians to prescribe certain brand-name drugs, and misleading advertising gave protesters more ammunition, as did challenges to the justice of high, and rising, drug prices when many companies spend more on sales and marketing than on research and development of new drugs.[12] Such publicity has severely eroded public trust in the industry.[13] It has been exacerbated by the environment of declining trust in corporations in general[14] and in conjunction with the prevalence of the enduring joke that business ethics is an oxymoron.

Starting in the 1990s, a few bioscience companies and BIO responded to this mounting criticism by seeking ways to include ethics as a part of their business strategy. Under Carl Feldbaum's leadership, BIO helped define an ethics agenda and mission statement for the industry, convened an ethics committee, and published an ethics brochure.[15] Ethics publications, papers, and books highlighted the benefits that could be obtained when business managers in this industry realized the ethical pitfalls associated with their products and included a consideration of

[11]Priest SH. US Public Opinion Divided over Biotechnology? *Nature Biotechnology.* 2000:18: 939–942.

[12]Angell M. *The Truth About the Drug Companies: How They Deceive Us and What to Do About It.* New York: Random House; 2004.

[13]Marsa L. *Prescriptions for Profits: How the Pharmaceutical Industry Bankrolled the Unholy Marriage Between Science and Business.* New York: Scribner; 1997; Grady D. (1998, April 15). Study Says Thousands Die from Reaction To Medicine. *The New York Times,* Section A1; Williams N. Food Safety: U.K. Government Tries to Reassure Wary Public. *Science.* 1998;282:856; DeAngelis CD. Conflict of Interest and the Public Trust. *JAMA.* 2000;284:2237–2238.

[14]Trust in Corporate American Has Hit Rock Bottom. *Harris Interactive.* February 24, 2004. Available at http://www.harrisinteractive.com.news.

[15]Bioethics: Facing the Future: There's More to Biotechnology than Science and Business. Available at http://bio.org.

ethics as a part of product development and marketing.[16] As individual companies sought to build an ethics capability that they often lacked internally, some hired outside ethics experts as consultants or employees. Others established ethics advisory boards to tap into a diverse spectrum of ethical perspectives—medical, religious, legal, and philosophical. Our collection of company cases features each of these approaches. The cases also feature ethics experts employed by bioscience companies, such as Steve Holtzman, who studied moral philosophy at Oxford before heading business development and ethics for Millennium Pharmaceuticals. Interleukin Genetics is another company with an affinity for hiring ethics experts with managerial responsibilities: Rahul Dhanda held a business-development position there while completing his book, *Guiding Icarus: Merging Bioethics with Corporate Interests.* Perhaps the most prominent example of such an individual is Phil Reilly, who began as an ethics advisor and board member for Interleukin and eventually became the firm's CEO.

The efforts by bioscience companies to address ethical issues, however, were greeted with a high degree of skepticism by the industry's critics. Allegations included the assertions that industry was "allowing corporate conundrums to masquerade as ethical problems,"[17] that companies were "buying a conscience,"[18] hiring ethicists to keep them honest,[19] merely enhancing the company's public image,[20] and using ethicists to preempt critics.[21] Biomedical ethicists who consulted for these companies drew similar criticisms. They were accused of allowing themselves to become coopted by the companies, of whitewashing for corporations,[22] of being "like watchdogs but...used like show dogs"[23] and not freely addressing complex issues.[24] Others wondered if the bioethicists were really performing as legal compliance officers.[25] Their motives were impugned and they were accused of profiteering as consultants,[26] and of being primarily interested in acquiring power, prestige, or money.[27,28,29,30]

[16]Brower V. Ethical Culture: Millennium Pharmaceuticals, Inc. *The HMS Beagle,* December 24, 1999; Dhanda, 2002; Eaton, 2004.

[17]Devries R. (2004, February 8). Businesses are Buying the Ethics They Want. *The Washington Post.* Section B2.

[18]Elliot C. Pharma Buys a Conscience. *The American Prospect.* 2001;12:16–20.

[19]Kerr K. (1999, June 5). Research Corporations Hire Ethicists to Keep Them Honest. *San Jose Mercury News,* Section 1E.

[20]Park P. Note 11, citing Virginia Ashby Sharp.

[21]Caruso D. Note 16, 1.

[22]Turner L. Note 12, 947.

[23]Elliot C. Note 14, 20.

[24]Michaels D, et al. Advice Without Dissent. *Science.* 2002;298(5594):703.

[25]Magnus D. Note 2, 385.

[26]Blumenstyk G. Bioethics Criticized for Lack of Policy on Their Own Industry Ties. *The Chronicle of Higher Education,* July 19, 2002.

[27]Younger SJ, Arnold RM. Who Will Watch the Watchers? *Hastings Center Report* 2002;32:21.

[28]Brower V. Biotech Embraces Bioethics; But Are They Being Exemplary or Expedient? BioSpace.com, 1999. Available at http://www.biospace.com/b2/Articles/061499_bioethics.cfm.

[29]Boyce N, Kaplan DE. And Now, Ethics for Sale? *US News & World Report,* July 30, 2001; Stolberg SG. (2001, August 2). Bioethicists Find Themselves the Ones Being Scrutinized. *The New York Times,* p. 1.

[30]Turner L. Bioethic$ Inc. *Nat Biotechnol.* 2004;22(8):947–948.

There are clearly instances in which corporate ethics programs have served as mere window dressing, but in most cases, companies appear to be making good-faith efforts to seek better ways to understand and handle the ethical issues they face. Within the industry and the organizations that represent them, there is a growing consensus among executives, physicians, and scientists about the wisdom of addressing the ethical aspects of their work. To address these issues competently, it seems wise to work in cooperation with biomedical ethics experts. As Dhanda has noted,[31] bioethicists and biotechnologists have much to learn from each other. As with any field of expertise associated with business activity, companies benefit most when the experts do not avoid them or capitulate to corporate interests, but rather assist in their operation, either from the inside or from the outside as consultants, by asking hard questions, and exploring the firm's underlying assumptions. Consequently, just as an appreciation for biomedical ethics has improved and enlightened the practice of medicine, human research, and hospital care, it now seems that a broader ethical perspective should also become a standard part of doing business in the bioscience industry.

A NEW APPROACH: BIOSCIENCE BUSINESS ETHICS

The goal of our project was to reveal and comment on the ways in which ethics is being incorporated into bioscience business ethics decision making. The research approach developed for this book, and the wider efforts of this project team,[32] are an effort to walk a middle path between the extremes of the critic safe in an ivory tower, too distant to offer practical guidance to the industry, and the entrenched in-house ethicist or consultant who may have a narrower experience that does not lend itself to forming wider conclusions. We tried to maintain research sensitivity through the use of a well-accepted qualitative research methodology for developing rich case-studies. At the same time, our independence from the firms and the ability to look at experiences across companies was intended to enable us to adopt an independent view, neither unduly critical nor too conciliatory. This balancing act is difficult, yet it seems to offer a way to provide in-depth analysis of the actors—bioscience companies—that are developing the new technologies that are raising the most challenging ethical issues.

To conduct our research, we assembled a highly interdisciplinary team of business school professors, legal scholars, sociologists, scientists, physicians, and graduate students. Our team is made up of researchers affiliated with the

[31]Dhanda, ibid.

[32]Among other activities, Stanford cases (Eaton, 2004) and KGI cases have been used to teach a business version of biomedical ethics to employees, business, and bioscience students. The CRDP at the Université de Montreal helped to develop an ethical approach to DNA databanks (http://humgen.umontreal.ca), and the Canadian Program at the University of Toronto Joint Centre for Bioethics has emphasized the potential benefits of biotechnology for developing countries.

Biosciences Business Ethics Center (BBEC), which includes professors from the Keck Graduate Institute (KGI) of Applied Life Science in Claremont, Calif., Stanford University, and the Université de Montreal, and those with the Canadian Program in Genomics and Global Health (CPGGH) based at the University of Toronto Joint Centre for Bioethics. The study was funded primarily with grants from the Seaver Institute to the BBEC and from Genome Canada to CPGGH,[33] with additional support from Genome Quebec to the Centre de Recherche en Droit Public (CRDP) of the University of Montreal. What follows is a brief description of our methodology.

Each case study focused on the ethical decision making processes in the company, and the ethical issues and mechanisms surrounding these processes. Our goal was not to identify companies that were representative of the bioscience sector, as many firms have no systematic process for dealing with ethical issues. Instead, we included companies that were adopting innovative and distinct approaches to ethical decision making, from which the rest of the industry might be able to learn valuable lessons. In addition, we sought a diversity of sector and geography, and of companies at different stages of growth. In all we invited 19 companies to take part in the project, and 13 agreed (see next section for brief descriptions of each of the 13 cases). Four pharmaceutical, one biotech, and one bioagricultural company declined. The participating companies covered the range of large and small biosciences companies in health and agriculture in the United States, Canada, and Europe. In the interest of full disclosure, we note that researchers on the project team had had prior relationships with some of the companies studied: the Centre in Toronto has received support from Merck and Co.; Peter Singer has received consulting funds from Merck Frosst and, subsequent to this study, from Genzyme Canada; and Margaret Eaton had accepted a small grant from Affymetrix for general research in business ethics 5 years prior to her work on this project.[34] To minimize potential conflicts of interest, researchers who had ongoing or past significant relationships with companies were not directly involved with that case's data collection, data analysis or write-up.

Data were collected between autumn 2002 and spring 2004. The primary source of case information was face-to-face interviews with more than 110 individuals in the companies. We worked with our main contact at each company to identify a list of participants who would cover most functional areas of ethical decision making in each firm: regulatory affairs, research operations, marketing, corporate affairs, corporate communications, human resources, clinical and laboratory operations,

[33]CPGGH also receives funding from the Ontario Research and Development Challenge Fund and other funding partners listed at www.geneticsethics.net.

[34]Bartha Knoppers and Abdallah Daar sit on Ethics Advisory Boards for other companies that did not participate in the study.

bioethics management, and corporate social responsibility management. Most interviewees were senior business leaders—the people most familiar with how ethics featured in the firm's strategic decision-making process—but frontline workers and lay people were also included. Wherever possible we used these individuals' own words to describe how they approach ethical issues. We aimed to have enough interviews to reach a point where we were hearing repeated information about the issues and mechanisms central to ethical decision making in that firm. Additional phone interviews were conducted when information was incomplete or when geographic constraints made face-to-face interviews impractical. The cases thus represent a "slice-of-time" look at company activity and are as accurate and current as we could make them up until the date written.

The interview data were supplemented with archival material gathered during the visits and from general research. Corporate sources included annual reports, ethics and values statements, press releases, official company policies and any evaluations conducted of ethics-related initiatives. We also obtained publicly available medical, professional, and lay material about the companies. These data were then analyzed, using a modified thematic analysis: that is, we identified key themes in why and how these companies had addressed ethics and what ethical issues they faced. Material and data were then incorporated by one team-member into a case write-up, which was then reviewed and edited by the other members of the team, as described in the first footnote of each case study.

Such detailed case studies require extensive cooperation from participating companies. To secure their agreement to take part in a project dealing with a highly sensitive subject, we allowed the company contacts to review the case write-ups to correct any perceived inaccuracies and remove any information they deemed to be confidential before publication, a common practice in business school case writing.

STRUCTURE OF THE BOOK

The case studies form the heart of the book. They show, in the kind of detail that current and future leaders in the industry should find useful, how 13 bioscience companies approach ethical decision making. Each case includes:

- an introduction to the primary ethical issues facing the firm
- a brief company history and business overview
- background explanation of the science or technology involved
- detailed discussion of the ethical decisions the firm must make as part of its strategy and operations
- a range of approaches the firm uses to make ethical decisions
- a conclusion identifying issues and questions for the future

Although the cases were written with narrative flow in mind, we attempted to address four key questions in each case: Why does this company address ethics?

What ethical issues does the company address? What mechanisms does the company use to address ethics? How effective does the company perceive these mechanisms to be, including whether any efforts are made to assess their effectiveness?

The cases are arranged in five thematic sections. Part 1 has four cases that introduce a wide array of ethical issues and show the vital role that a company's early leadership plays in shaping the organization's approach to ethical issues. The first case is *Merck,* one of the world's largest pharmaceutical companies, and one that has been a leader in adopting an ethical approach to this competitive global industry. The case examines how Merck, at a time when the corporation and its leaders were under growing pressure from the investment community, was able not just to sustain, but to significantly increase its ethics and corporate social responsibility programs. The Merck case study explores the variety of mechanisms and initiatives—an internal ethics office, the creation of Ethics Centers around the world, the charitable programs of the Merck Foundation—that Merck uses for ethical decision making.

We then examine *Genzyme,* the world's fourth-largest biotech company, and a leader in the development of ultra-orphan drugs that treat rare genetic disorders suffered by 10,000 or fewer patients worldwide. This case considers how Genzyme's strategic focus on "putting patients first" has shaped its approach to a wide array of ethical challenges, including drug pricing and access for treatments that can cost $200,000 a year for the rest of the patient's life; how to conduct an ethical, placebo-controlled trial for a drug that is already on the market; how to deal with personal conflicts of interest when managers or employees have relatives who need treatment for these rare disorders.

The third case is *Millennium,* one of the most successful of the second generation of biotech companies, and arguably the leading voice for ethical behavior in the biotechnology industry. The importance of ethical issues was first articulated by the CEO and evident from the outset of this Cambridge, Massachusetts-based firm when it hired Steve Holtzman to be both its Chief Business Officer and in-house ethicist. The case study traces the approach to ethics decision making over the firm's 10-year history, and the many innovative strategies that it has used to make ethics a key focus. Among them are a movie-discussion series on ethics; instilling the company's core values into every corporate program; an ethics helpline; and hiring ethics experts to run ethics education workshops within Millennium.

This section concludes with *Maxim Pharmaceuticals,* a San Diego-based bioscience firm that develops drugs from naturally occurring histamine. The case highlights the vital role that the firm's CEO, Larry Stambaugh, has played in shaping the firm's core values and innovative approach to good corporate governance. The case concludes by exploring how the CEO and board deal with a series of business and ethical challenges posed by efforts to raise financing that are complicated by the passage of the Sarbanes-Oxley Act.

In Part 2, we look at companies that are facing ethical issues specific to the environment and to the use of animals in research. *Diversa,* a San Diego-based company, has been a pioneer in the development of benefit-sharing partnerships that align with the goals of the Convention on Biological Diversity. As a leader in

this area, however, it also has become a lightning rod for critics of public and private sector partnerships, inhibiting its ability to collect genetic samples. The case examines the rationale for Diversa's biodiversity collaborations and how these agreements operate. This is followed by *Pipeline Biotech*, a contract research organization (CRO) located in a rural part of Denmark that specializes in conducting animal studies for drug companies. The case focuses on how this start-up enterprise has grown, thanks in part to the controversy surrounding animal testing in England and the eagerness of UK-based companies to outsource this work to another part of the European Union with a friendlier regulatory and societal climate for such research. It also illustrates the distinctive approach to ethical issues that Pipeline has adopted—delegating decision making to the frontline laboratory technicians who are empowered to end any experiment if they feel an animal is not being treated ethically or humanely. The last case in this section deals with *TGN*, an early-stage Canadian company trying to build a sustainable approach to ethical decision making in preparation for the challenges to its controversial transgenics business: producing human proteins in, and then extracting them from, pig semen.

Part 3 focuses on an emerging field in the bioscience industry that bridges health and nutrition. Nutrigenomics has developed since the sequencing of the human genome, as companies seek to analyze individuals' genetic information to provide guidance on disease prevention through diet and on effectiveness of medication when treatment is necessary. *Interleukin Genetics* is a Waltham, Massachusetts-based company that made the unusual decision to appoint an ethics expert, Dr. Phil Reilly from Harvard, as CEO. Reilly and his leadership team were faced with an ethical challenge when their firm was in danger of running out of money: should they accept a takeover offer from Alticor, the parent company of Amway, to transform their firm into a nutrigenomics firm? *Sciona* is a UK-based company that advertises and sells direct-to-consumer nutrigenomics services on the Internet. This case study, instructive in several ways, highlights ethical issues related to genetic testing in the very new field of direct-to-consumer marketing of genetics services; a bioethics-consultant model of addressing these issues; and the interaction between a firm, NGOs, and a government commission.

Part 4 examines how companies have sought to enhance their decision making by seeking the advice of diverse ethical experts. *Affymetrix*, a Silicon Valley-based company that has been a pioneer in the development of gene chips, has created an ethics advisory committee to advise them on the many ethical issues involved in the appropriate use of human genetic information. *PharmaSNPs* (a pseudonym we used because the company was taken over during our research), was a genomics firm focused on identifying genetic linkages with major diseases; it gathered human genetic data from around the world through CROs and tried to develop clear ethical guidelines on how to conduct this research. The case study focuses on the ethics advisory board it created to aid in this effort.

Part 5 examines one of the greatest challenges that any company faces in dealing with ethical issues: assessing whether its particular approaches are effective.

Monsanto, the leader in the commercialization of GM crops, became the focal point for critics of GM products. This criticism was so strong that it had a major impact on the company's ability to operate in Europe and other parts of the world. The case study describes how Monsanto made major changes in its approach to ethical issues in response to these critics. These changes included the adoption of a new, detailed reporting system to track its performance against a new ethics guide, the *Monsanto Pledge*. The final case is *Novo Nordisk*, a Danish firm that has been a world leader in the treatment of diabetes, which has relied on stakeholder involvement and the use of its "Triple Bottomline" to assess both its social and its business performance.

The concluding chapter analyzes the findings across the 13 cases. It observes the patterns in the ethical issues facing bioscience firms and how these vary across sectors and stages of firm development. It presents a framework that integrates the different mechanisms firms use for dealing with ethical issues. The analysis highlights lessons learned from the experiences of these leading companies and some of the issues that the bioscience industry may face in the future.