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Challenges for Corporate Ethics in Marketing Genetic Tests

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ABSTRACT. Public discussions of ethical issues related to the biotechnology industry tend to treat ''biotechnology'' as a single, undifferentiated technology. Similarly, the pros and cons associated with this entire sector tend to get lumped together, such that individuals and groups often situate themselves as either ''pro-'' or ''anti-'' biotechnology as a whole. But different biotechnologies and their particular application context pose very different challenges for ethical corporate decision-making. Even within a single product category, different specialty products can pose strikingly different ethical challenges. In this paper, we focus on the single over-arching category of ''genetic testing'' and compare tests for disease susceptibility and drug response. We highlight the diversity of ethical challenges – grouped under the broad categories of ''truth in advertising'' and ''protecting intellectual property'' – raised by the commercialization and marketing of these technologies. By examining social and technical differences between genetic tests, and the associated corporate ethics challenges posed by their commercialization, our intent is to contribute to the nascent business ethics literature examining issues raised by the development and marketing of genetic tests.

KEY WORDS: biotechnology, genetic testing, disease susceptibility, pharmacogenomics, corporate ethics, business ethics, marketing, commercialization, intellectual property rights, truth in advertising

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Introduction

There is substantial public and media interest in the potential benefits and risks of biotechnology. Rarely does a day pass without seeing news stories about the discovery of novel disease genes, the funding of large-scale genomics research initiatives or the development of promissory biotechnologies. Genetically modified organisms, biotechnologically derived medicines and genetic tests are held up as ''revolutionary'' applications of knowledge from ''the book of life''. But these same technologies are also cause for serious concern, as for some critics they are examples of unacceptable hubris in which scientists are ''playing God'' and putting society at ''risk'' by unleashing ''Frankenstein'' creations (Hellsten, 2005). In such discussions, there is an unfortunate tendency to treat biotechnology as a single, undifferentiated category or class of technology developed by a monolithic biotechnology industry. Similarly, the diversity of pros and cons of various biotechnologies (whether related to the technology, its application platform or the industry)

are often lumped together such that individuals and groups situate themselves at the polar extremes of a debate – as if one must be either entirely ''pro-'' or entirely ''anti-'' biotechnology.

Different biotechnologies, however, raise different socio-ethical and policy questions, and the importance of these will vary for the different stakeholders involved. The questions raised by the introduction of genetically modified (GM) foods in North America and Europe (e.g., concerns about environmental impact, benefit to farmers and consumers, or effects on developing countries) are different from those posed by the application of gene therapies (e.g., safety, effectiveness, access to services). The stakeholders in the GM food debate (e.g., consumers, farmers, food retailers, agricultural biotech companies) are very different from those involved in the development of gene therapies (e.g., patients, advocacy groups, clinicians, biotechnology companies, regulators). Even within a single product category, different specialty products can pose strikingly different ethical challenges. In this paper, we compare the marketing of two types of commercial genetic test – for disease susceptibility and for drug response – and highlight two broad areas that raise diverse challenges for corporate ethics, specifically (1) truth in advertising, and (2) protection of intellectual property rights. Comparing these two related technologies is sufficient to demonstrate the need to avoid lumping all biotechnologies together in our ethical assessments.

As we examine the diversity of stakeholders, interests and product-specific socio-ethical challenges involved in two different kinds of genetic tests, we also ask ''what is a well-intentioned biotechnology company or corporate decision-maker to do?'' By examining social and technical differences in the genetic tests, and the associated corporate ethics challenges posed by their marketing to the general public, our intent is to contribute to the nascent business ethics literature examining issues raised by the commercialization of genetic tests.

Selling genetic information

The term ''genetic testing'' has been used to refer to a variety of diagnostic or predictive technologies for analyzing a person's genetic make-up. These tests function by analyzing the DNA in a person's blood or other biological material in order to identify changes in the structure of a particular gene or the level of its expression in different organs. Genetic tests are being used, among other applications, to diagnose hereditary diseases, to provide information about susceptibility or risk of developing a disease, to evaluate the likelihood of a person's positive or negative reaction to a medication and to identify an individual and/or their relatedness to others.

Until relatively recently (i.e., the last 15 years), genetic tests were restricted to medical or forensic institutional settings – they were developed in university research laboratories and then applied in medical genetics departments or police forensics units. Increasingly, genetic tests are being commercialized by biotechnology companies eager to capitalize on the knowledge and technologies arising from the Human Genome Project, completed in 2001. Facilitated by the rapid and global expansion of the Internet, the last decade has seen a burgeoning consumer marketplace for health care information and products, and genetic tests are now just one of a plethora of health care services being marketed to medical professionals and consumers alike. Consumers can now purchase genetic tests for health and nutritional status (Chadwick, 2004), paternity (Belluck, 1997; Kaebnick, 2004), disease susceptibility and drug response (Gollust et al., 2003; Williams-Jones, 2003), and these tests are often marketed as being no more worrisome than other, much more traditional, commercially available diagnostic kits (Lewis, 2001).

Whether a person is interested in monitoring their blood glucose or cholesterol levels, knowing their HIV or pregnancy status, determining their risk of developing a disease or having a negative reaction to a prescription drug, what they are seeking is information. However, the application of these diagnostics tests, and interpretation of the information they provide, may not be simple or straightforward. In some cases, e.g., very accurate pregnancy or paternity tests, the results are ''black or white'' and easy to interpret – a person is either pregnant or not, is or is not the father; how one then deals with this information may nonetheless be extremely challenging. For other tests, such as those for genetic susceptibility to disease, the results themselves are often ''gray'' – the information is about *risk* rather than certainty of developing a disease and there may be significant scientific uncertainty about the technical accuracy of the test itself.

Thus while a person's desire for information, e.g., to help inform health care decision-making, may be similar across a range of diagnostic tests, the accuracy of the test and the utility of the resulting information can vary enormously. This situation poses strikingly different challenges for different kinds of decision makers, including consumers, health professionals, and corporate managers.

Beginning with brief fictional case studies, the following sections examine and compare two types of genetic test – those that test for disease susceptibly and those that test for drug response – and then explore the implications each has for decision-makers at biotechnology companies.

Testing for genetic susceptibility to disease: intro

> Veritas Diagnostics is a biotech company specializing in genetic susceptibility tests for a range of conditions, including cystic fibrosis and hereditary cancers. It has a well-staffed and sophisticated molecular genetics laboratory, is committed to implementing the highest quality technologies, and is known for providing accurate and confidential services at a competitive price. Keen to expand its existing client base (hospitals), Veritas has begun marketing its services direct to consumers. According to the company Vice President, the only ethical issue at stake is consumer privacy, which is already addressed by the company's strong confidentiality policy and data management practices. The company's Ethics Officer, however, is concerned with broader questions relating to the need for genetic counseling, the limitations inherent in the predictive value of test results, collaboration with local and national health care institutions, etc.

As biotechnology companies, such as the fictional Veritas Diagnostics, begin marketing their services to the general population, they will face a host of technical, social and ethical challenges; and to a certain extent, these challenges are due to the hereditary nature of genetic information (with implications for extended family members or future offspring) and the inherent limitations in the accuracy of genetic tests.

Genetic susceptibility tests can be very useful to individuals and their families because they can provide information that can aid in disease management, permit choices about lifestyle or family planning, and reduce anxiety about disease risk. Yet much uncertainty remains. How should clinicians tell prospective parents about their chance of having a child with a hereditary disease? If the diagnosis is relatively certain, are preventative or treatment options available? A person may be identified as being at *increased risk* and still never develop the disease, so how should patients and families deal with such uncertainty (Codori, 1997; Hutson 2003; Prospero et al., 2001)?

Further, even the best genetic susceptibility tests are not 100% accurate or informative for all people. Differences in laboratory procedures, limitations in scientific knowledge, and diversity in individual genetic make-up mean that test results may be (1) false positive (a person *does not* actually have the disease mutation but the test suggests they do); (2) false negative (a person *does* have the disease mutation but the test suggests they do not); or (3) uninformative (a person has a previously unidentified mutation). For example, Myriad Genetics' BRACAnalysis test analyses two genes (BRCA1 and BRCA2) associated with greatly increased risk for breast cancer. However, only 5–10% of women who develop breast cancer have a hereditable form of the disease (i.e., have an inherited genetic mutation), and of this 5–10%, the test will detect only 17–25% – so for roughly three-quarters of women tested, the genetic causes of their disease remain unknown (Frank et al., 2002; Shih et al., 2002; Szabo and King, 1997). And even for those women in whom a BRCA mutation is detected by Myriad's test, the results are not always accurate – they may receive false results because the test could not detect their particular BRCA mutation, or because their form of the disease was caused by another gene not analyzed by Myriad's test (Walsh et al., 2006).

In light of these scientific and technical challenges, genetic susceptibility tests have historically been delivered through public and private health care systems. Health care professionals, usually medical geneticists and genetic counselors, work with patients and families to evaluate and explain the utility and limitations of a genetic test and determine what other health care services (e.g., treatments, monitoring, etc.) may be needed. But as already mentioned, individuals can now purchase a diversity of genetic tests online, sometimes with little clinical

involvement or counseling support. Patients, as consumers of health care services, are increasingly in the position of deciding whether they want a particular genetic test, and acquiring access to such tests for reasons that may be important to them but which may be considered ''clinically not relevant'' by medical professionals because the tests fail to contribute to diagnosis, prevention or treatment of a disease. Genetic testing has thus ''drifted'' from the clinic to the marketplace (Williams-Jones and Graham, 2003).

Clearly, even a well-intentioned biotechnology company such as ''Veritas'' will face some serious issues in marketing such a technology. Given the informational uncertainty associated with many genetic tests, what responsibilities (especially with regards to information content and counseling support) does Veritas have towards its customers? How can the company protect its intellectual property, recoup its R&D expenditures and show a profit, and also be an ethical company when there may be only limited consumer demand for genetic tests that do not offer a definitive diagnosis but merely a ''risk profile''? These questions have presented serious challenges for real-world biotech companies such as GeneDx, Myriad Genetics or, Athena Diagnostics, that are offering commercial genetic testing services (Williams-Jones, 2003).

Testing for susceptibility: truth in advertising

In order to expand what is often a relatively small market for genetic services – ''small'' because tests have typically been directed at families with rare hereditary diseases – there has been a tendency on the part of many diagnostics companies to downplay the probabilistic nature of genetic information and to use *deterministic* language in their physician- and patient-oriented advertising and promotional campaigns. A prominent example is Myriad Genetics' direct-to-consumer marketing of their BRACAnalysis test (Gollust et al., 2002; Mykitiuk, 2004). In their TV advertisement, the inevitability and fear of developing breast cancer – ''I wondered if it would be inevitable...it didn't have to be'' – is challenged and remedied by the *certainty* of a test that accurately links genetics with risk. ''BRACAnalysis can help you see the big picture so you can take steps to reduce your risk.'' Personal medical concerns are thus raised and ostensibly resolved by subsequent offerings of genetic technologies (Williams-Jones, 2006).

Now one might reasonably ask, ''What is the harm in marketing a genetic test that only provides risk information? It's not as if the consumer is purchasing a potentially toxic prescription medication without professional advice!'' Put more forcefully, one could argue by analogy that as people clearly have the right to spend their money on frivolous and harmless activities such as having their fortunes told at a carnival, people should also have the right to purchase genetic tests. After all, these tests *merely* provide information about disease risk, so even if the test is not clinically indicated and may well be inaccurate, what is the harm? And if there are no serious risks involved in buying genetic tests, then it would seem that their sale must be ethically permissible (Burgess, 1999).

Purchasing a genetic susceptibility test, however, is not the same as paying to have one's fortune told. The latter is arguably a waste of money, but will cause little harm and can be easily justified as entertainment. By contrast, genetic susceptibility tests can cost hundreds or thousands of dollars and the resulting information is far from innocuous. If one considers that genetic test results may be used to plan whether one has children, undertakes preventative surgery, or continues with or ceases regular disease monitoring, it becomes clear that the impact of misleading or inaccurate information can be profound. Genetic information can also lead to discrimination (e.g., in seeking employment, or health and life insurance) and even stigmatization of certain ethnic groups or communities (Gillam, 1999; Hall and Rich, 2000; MacDonald and Williams-Jones, 2002).

Despite these concerns, a biotechnology company such as Veritas may have a strong interest in promoting and even hyping the utility and accuracy of their genetic tests. Unlike the rare hereditary diseases such as Huntington's, for which patient populations – and thus the potential market – will be relatively small, the entire human population has the potential to be affected by common complex diseases such as cancer or heart disease. So if a company has a patented genetic test for a rare hereditary form of a

disease (e.g., one of the hereditary forms of breast cancer), it may be in their economic interest to market this test to as large a part of the population as possible, i.e., to a population that includes anybody at risk for or worried about the non-hereditary form of the disease. If the market is too small, then one simply needs to expand it!

One way of building a market for a genetic test is to tie it, in the minds of potential customers, to pre-existing fears about disease, while also emphasizing the causal role of genetics to the exclusion of other social or environmental factors. As in the Myriad advertising, reductionist marketing paints the disease in question as being largely ''genetic'', depicts the test results as essentially black or white, and asserts that through using the test consumers can become ''empowered'' to make informed decisions (Mykitiuk, 2004; Williams-Jones, 2006). But biotech companies must be wary about over-playing the benefits and minimizing the limitations of their products, if they are not to run afoul of government oversight agencies. For example, the U.S. Food and Drug Administration and Federal Trade Commission have the remit to fine companies and require changes in advertising – although these agencies have yet to do so in the case of genetic testing (Caulfield et al., 2001) – for providing misleading or inaccurate advertising. There is a fine line between positive promotion and unsubstantiated hype, especially for a technology as poorly understood by the public as genetic testing.

Concerns about inappropriate advertising and marketing of genetic tests have led to calls for increased government regulation of laboratories, closer scrutiny of advertising claims, and even the outright banning of commercial genetic services (Bowen et al., 2005; GeneWatch UK, 2003). In this context, corporate decision-makers are faced with the challenge of legitimately promoting their service to as large a market as possible while not overstating their claims. Moreover, if one accepts that genetic information can be potentially harmful, companies must also decide whether they should encourage or even provide counseling services to their clients – do companies have a responsibility to their clients beyond the provision of accurate genetic information? Should a company provide counseling services themselves, or can these services be provided by health professionals? Should counseling be required as part of the testing process? Could this service be contracted out to private genetic counselors, and what about potential conflicts of interest (MacDonald, 2002)? The provision of genetic information is not a simple endeavor, and is one that raises difficult practical and ethical questions for corporate decision-makers.

Testing for susceptibility: protecting intellectual property

The discovery of the genes associated with hereditary or common complex diseases has come about after decades of costly public and privately financed research. While recent technological advances have significantly reduced the time involved in gene discovery, it often still takes years before the necessary clinical and population data are available to confirm the link between a gene and a disease, and then to allow for the transformation of a patented ''disease gene'' into a marketable genetic test. Once developed, the technologies at the core of many genetic services, that is DNA sequencers, are also extremely expensive and require highly trained technical staff and advanced laboratory facilities. This means that the unit cost per genetic service has tended to be quite high. In order to cover costs and generate a profit, many biotechnology companies have priced their genetic tests in the two to three thousand dollar range. At such high prices, and especially given the uncertainty often associated with the resulting genetic information, many susceptibility tests have proven far too expensive for average consumers. Similarly, cost-effectiveness considerations and limited budgets have meant that health care institutions and health insurers have covered only a limited number of tests for circumscribed patient populations (British Medical Association, 2005; Ho et al., 2003).

It should not be surprising, then, that the commercialization of genetic susceptibility tests (whether sold to health insurers, hospitals or individual consumers) has proven rather difficult – genetic information has simply not been a good ''product''. As discussed above, some biotechnology companies have tried to develop markets for their proprietary genetic susceptibility tests by advertising to the general public, but restrictions on direct-to-

consumer advertising in most countries (with the exception of the U.S. and New Zealand), and the high costs of tests have meant that companies have had limited success. Nevertheless, and in part facilitated by the Internet and global media access, direct-to-consumer advertising for and access to genetic tests continues to flourish (Williams-Jones, 2003, 2006).

One somewhat successful approach to creating a market has been the strong defense of patent rights. Gene patents give diagnostics companies substantial power to control the development and application of genetic tests. A company may license their proprietary technology to a university diagnostics laboratory or health care institution, so that the institution must pay a fee to use the proprietary technology to provide services to their clients. A company can also use their monopoly rights to force (i.e., by threatening suit for patent infringement) laboratories or health care institutions to contract-out genetic services that would then be conducted in company laboratories. This latter approach – exemplified by Myriad Genetics, among others – has proven quite successful in the U.S., where most public and private health insurance plans now cover the costs of accessing a diversity of commercial genetic tests. However, this approach has met with significant resistance and very limited success in Canada and Europe. Their universal health care insurance systems, and a general public and government reaction against a U.S. company (i.e., Myriad) enforcing their patent rights, has meant that many provincial and national governments have rejected or ignored gene patents and refused to purchase costly commercial genetic tests. Instead, hospital laboratories in Canada and Europe have continued to perform genetic tests in-house (testing was in the public domain prior to the granting of Myriad's patents) and provide services through their public health care facilities (Cho et al., 2003; Verbeure et al., 2005).

In trying to protect their intellectual property rights, biotech companies may actually undermine their ability to develop functional markets for their costly genetic technologies. Other stakeholder values, such as a commitment to ''public health care'', may have disproportionate influence on institutions and policy makers. By not taking such values into account and simply attempting to enforce their patent rights, companies may alienate what would otherwise have been very large health care consumers; in Canada and Europe, it is not individual patients but instead the provincial and national health insurance programs that purchase the vast majority of genetic tests. In pushing for the adoption of expensive tests by health care insurance plans, tests that in some cases are double or triple the cost of services performed by public laboratories, diagnostics companies have been accused of profiteering and threatening the continued public provision of affordable genetic services. Corporate decision-makers are thus faced with the serious business ethics challenge of, on the one hand, protecting their intellectual property rights and selling their services for a reasonable profit, while on the other hand trying to avoid the charge of profiteering and also respecting diverse local/national values that may go against standard business models based on maximizing corporate revenues. For a company to effectively enforce its intellectual property rights regarding a genetic susceptibility test while behaving in an ethically responsible manner is thus no easy task.

Testing for drug response: intro

Pharmacogenomics is a field of biomedical research predicated on the view that a better understanding of how individuals and populations vary genetically in their response to medications will help to rationalize the choice of drug dosages or the drug itself, enable the development of safer and more effective drugs, and ultimately lead to personalized medicines. The following fictional case provides an example of some of the goals and challenges faced by biotechnology companies seeking to market pharmacogenomic technologies.

> PGx Ltd is a small biotech company focused on developing pharmacogenomic tests for a diversity of enzymes and metabolic pathways linked to drug response. One of PGx's latest tests identifies genetic variations associated with strong or weak response to a class of drugs linked to appetite suppression, one of which is Hygea Pharma's new anti-obesity drug, currently in the final stages of clinical research. Given the widespread public attention to the ''obesity epidemic'' and the rush on the part of the pharmaceutical industry

to bring anti-obesity drugs to market, PGx's pharmacogenomic test may prove a very popular and profitable technology. The managers of PGx have been in discussion with Hygea Pharma and are struggling to decide whether they should go it alone and market their test to the general public, sign a licensing agreement with Hygea Pharma, or even negotiate a buy-out of PGx entirely.

An important driver behind the development of pharmacogenomics is the fact that many of the drugs people take do not have the anticipated positive therapeutic effects. While many drugs are clearly beneficial and even life-saving, *only about 50%* of patients actually respond positively to their medications (Spear et al., 2001); of serious concern, then, are the remaining 50% of patients for whom their medication is either ineffective or toxic. In the U.S., for example, adverse drug reactions (ADRs) are responsible for 106,000 patient deaths each year (Lazarou et al., 1998). The aim of biotech companies such as the fictional PGx Ltd., then, is to understand the genetic factors involved in ADRs and drug response more generally, and then to deploy technologies to ensure that people only receive drugs that are safe and effective.

Specifically, pharmacogenomic tests are being developed by biotechnology and pharmaceutical companies to: (1) identify genetic markers to categorize patients into groups that will or will not benefit from certain medications; (2) identify genetic sub-types of disease and match these with particular drugs; and conversely, (3) examine partially developed but un-commercialized drugs to see whether they can be safely used for particular patient groups (Ozdemir and Lerer, 2005). Pharmacogenomic health care products thus involve a two-step process: (1) a genetic test is used to identify a person's genetic make-up so that (2) a specific medication can be administered. Prominent examples of pharmacogenomic drugs for which there are associated genetic tests include Abacavir for HIV/AIDS, Herceptin for metastatic breast cancer, and Gleevac for chronic myelogenous leukemia.

While there have been important developments in the field of pharmacogenomics, there has also been substantial rhetoric and hype from the biotech and pharma industries, patient advocacy groups, etc., about the substantial and soon to be realized benefits (Williams-Jones and Corrigan, 2003). Advocates argue that not only will pharmacogenomics revolutionize patient care by ensuring the provision of safe and effective drugs, it will also enable biotech and pharmaceutical companies to develop profitable and sustainable markets. But when the promises behind the rhetoric are not realized, the consequences for corporate decision-makers can be very serious – as witnessed with the hype surrounding gene therapy and the early biotech companies, when functioning products fail to materialize as promised, investors will abandon a field of innovation and make future venture capital very hard to raise (Fleising, 2001).

Testing for drug response: truth in advertising

Although pharmacogenomic derived medications are still relatively rare, there is a developing market for genetic tests that can predict drug response. Biotech companies, such as Vysis Inc., a subsidiary of Abbott Laboratories, are actively marketing pharmacogenomic tests to the general public and health professionals (e.g., Vysis' PathVysion test, which evaluates breast cancer patients' likelihood for a positive response to Herceptin). But a biotech company may also, as in the PGx Ltd. case study, consider marketing their pharmacogenomic tests to the pharmaceutical industry, and for two rather different ends. They may seek to convince a pharmaceutical company to: (1) buy or license the pharmacogenomic test to link with an already marketed drug, or (2) buy the entire biotech company so that the pharmaceutical company can have an in-house test development and delivery capacity. To further complicate matters, various pharmaceutical companies are also developing pharmacogenomic tests in-house, and they likely have very different interests from those of biotech companies (Eisenberg, 2002). Thus depending on the stakeholder, there may be significant differences in how and to whom pharmacogenomic tests will be marketed.

As is the case for genetic susceptibility tests, pharmacogenomic tests have limits that must be considered by corporate decision-makers. A pharmacogenomic test may be useful in some circumstances, but not work for all drug candidates. Cancer

is an example of such a situation. There is no one disease called ''cancer'', and even within sub-categories such as breast or colon cancer, there are a diversity of disease types and potentially appropriate medications. In this situation, a biotech or pharmaceutical company with a pharmacogenomic test may try either to market their product for an entire sub-category of cancer (e.g., breast cancer), thus potentially overstating the utility of their test. Roche Molecular Systems, for example, markets their *AmpliChip CYP450* to predict the activity of two drug metabolizing enzymes (CYP2D6 and CYP2C19). It is worth noting that this pharmacogenomic test is marketed to physicians (who often have little formal training in genetics) and to patients in a *context free* fashion, not linked to a specific drug or disease. The suggestion is that this test will benefit patients who are being prescribed drugs that are subject to metabolism by the aforementioned enzymes. However, variable metabolism does not, in and of itself, always translate into clinically significant differences in drug effectiveness or toxicity. These nuances mean that each pharmacogenomic test, its clinical utility and cost-effectiveness may have to be reconciled with reference to a specific drug, the target disease and the presence or absence of alternative medications that are not subject to genetically variable metabolism. Context free marketing of pharmacogenomic tests broadens the commercial markets but also carries the risk of misinforming patients and consumers about the *projected* and *actual* value of the test in clinical decision-making.

A company such as PGx Ltd. might also target their pharmacogenomic test at a specific sub-type of the disease and its associated treatment, such as Hygea Pharma's anti-obesity drug. But while this may be beneficial for patients, it could be counter to the commercial interests of the pharmaceutical company supplying the medication, particularly if the pharmacogenomic test rules out their drug for some patients and instead favors a competitor's drug. Pharmacogenomic tests can thus fragment both the disease and patient categories to which the pharmaceutical industry has traditionally directed its blockbuster drugs; as will be discussed in the following section, this can influence a pharmaceutical company's willingness to commercialize already patented pharmacogenomic tests.

Even when the pharmacogenomic test is designed to identify those people with a specific condition who can benefit from a particular drug (e.g., Abacavir for HIV/AIDS) while avoiding known life threatening side effects, the test itself cannot replace the need for judicious clinical monitoring. A fundamental weakness of pharmacogenomic tests is that they test a person's genetic make-up once and the resulting information is then used to determine their response to a particular drug. But it is proteins that are the workhorses of the body, that metabolize drugs and on which drugs operate; importantly, these (protein) effects or actions are not static, but vary over time (Kalow, 2006). Thus, because pharmacogenomic tests do not directly test protein function, they can provide limited certainty about how a person will react to a drug over the ensuing days, weeks or months of a treatment plan. A person may initially respond positively to a pharmacogenomically selected medication and then still develop toxic side effects at a later date when protein function is modified by environmental factors such as diet or drug–drug interactions.

These limitations, and the diverse patient and corporate interests involved, can pose serious challenges for biotech companies seeking to market their pharmacogenomic tests. Should PGx Ltd. downplay the scientific limitations of their product and market it to as large a population as possible (e.g., all those people identified as overweight), or focus on specific patient or disease subgroups where the technology will be more accurate (Reidenberg, 2000)? If they opt for the latter, how then do they interact with (or counter) the potentially very strong interests and power of Hygea Pharma to control drug development and marketing for the largest attainable segment of the patient population (Sherrid, 2001)? Or should PGx Ltd. simply ''sell-out'' to Hygea Pharma and allow them to decide how a paired pharmacogenomic test and drug will be marketed, and to whom?

Testing for drug response: protecting intellectual property

As briefly mentioned above, by identifying genetic differences in individual and group response to drugs, and the interaction of drugs with disease

types, pharmacogenomics fragments patient and disease groups. This fragmentation has significant, and very different, implications for biotech and pharmaceutical companies and the markets they seek to control.

The pharmaceutical industry has shown interest in upstream drug discovery oriented pharmacogenomic applications (i.e., those used in R&D) because of the anticipated expiry over the next several years of a large number of patents that ordinarily provide market exclusivity for blockbuster drugs (i.e., drugs that generate more than $1 billion in revenue) (Angell, 2004; Service, 2004). Pharmaceutical companies are finding it increasingly difficult to develop new blockbuster drugs (Horrobin, 2000), and most of those currently in development are ''me-too'' drugs, differing only enough from drugs already on the market to enable patent protection (Center for Drug Evaluation and Research, 2005). So the hope for many in the pharmaceutical industry is that pharmacogenomics will facilitate the identification of disease genes as targets for new drugs, and even allow companies to ''risk-proof'' their drug development pipelines so that those drugs that do get to market do not later turn out to be unexpectedly toxic, leading to costly post-marketing withdrawals.

Pharmacogenomic tests, however, can also threaten the traditional and still highly profitable blockbuster model of drug development, and thus not surprisingly not all pharmaceutical companies (or even all departments within a company) are uniformly enthusiastic about pharmacogenomics (Williams-Jones and Corrigan, 2003). No longer can one or only a few companies dominate a disease category: biotech or other pharmaceutical companies marketing their proprietary pharmacogenomic tests will create niche patient populations and disease categories. Instead of having a ''one-size-fits-all'' effective but suboptimal anti-obesity drug, companies like the fictional Hygea Pharma will be faced with a fragmented disease market and consumer demand for better predictability of drug effectiveness and toxicity (Danzon and Towse, 2002). This may then increase competition among pharmaceutical companies (and biotech companies developing their own novel drugs) for ever shrinking and fragmenting patient population and disease markets.

In this context, pharmaceutical companies may have very strong interests in patenting tests linked to their drugs, even if they may have no clear intention of commercializing them, in order to prevent competitors from developing technologies that could threaten the blockbuster model (Sherrid, 2001). In other words, protectionist patents ''upstream'' at the research stage could be used to block ''downstream'' technology development in the form of genetic tests that would ultimately benefit patients (Eisenberg, 2002; Ozdemir et al., 2006; Williams-Jones and Ozdemir, 2006). By contrast, biotechnology companies have an interest in patenting pharmacogenomic tests and fragmenting drug and disease markets, but may not have the research or financial capacity to go up against the very large pharmaceutical companies. Well-intentioned biotech companies such as PGx Ltd. may thus feel pressured to ''play along'' with the pharmaceutical industry in preventing or at least slowing the development of beneficial pharmacogenomic tests. Ethical challenges arise not only from ''commission'' but also from ''omission''. Yet the socio-ethical consequences of the unavailability of genetic tests may remain unrecognized by consumers, academic investigators or regulators. Would PGx Ltd., then, still have a responsibility to ensure that their costly gene patents are *actually* translated into commercially available genetic tests? Of course, a duty to commercialize would be hard to argue for in a free market economy. But companies that choose not to market a potentially useful product ought to face that fact and associated ethical corollaries candidly.

Conclusions and future perspectives

As should be clear by this point, different biotechnologies raise very different social and ethical concerns for the diversity of stakeholders involved in their development, application and/or rejection. One need not go so far afield as to compare the problems faced by Monsanto in their marketing of GM agriculture with those faced by companies trying to commercialize gene therapies. Even a brief examination within one particular category of technology, e.g., genetic testing, shows that a diversity of corporate ethics challenges can arise. This being the case, if corporate or business ethics reflection on the issues associated with developments in biotechnology are to be relevant, the focus of

analysis must be on individual technologies. At this higher resolution of analysis, it then becomes possible to identify the key tensions, interests and values at play, and then to propose methods or mechanism that might resolve these challenges.

In the case of commercial genetic testing, there has been significant discussion and debate in the bioethics literature about the various problems posed by the marketing of these technologies, for patients, health professionals and policy makers (Caulfield, 2005; Human Genetics Commission, 2003; Ratcliff, 2003; Williams-Jones and Burgess, 2004). But there has been relatively little discussion about the challenges faced by well-intentioned biotechnology companies or their corporate decision-makers (notable exceptions include Dhanda, 2002, 2004; Finegold et al., 2005). In this paper, we have sought to add to this latter discussion by highlighting some of the important ethical challenges – grouped under the broad headings of ''truth in advertising'' and ''protecting intellectual property'' – raised by genetic tests for disease susceptibility and drug response. We have not proposed specific means of resolving these various challenges, as they are each in need of detailed analysis. Instead, our hope is that readers will be convinced of the need for such thoughtful reflection on the part of business ethics scholars, and the potential for constructive application of the theoretical and practical tools of this field of applied ethics to a hitherto under explored area, the study of commercial genetic testing.

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