Information Assurance and Security Ethics in Complex Systems: Interdisciplinary Perspectives

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Chapter 9
Ethics, Privacy, and the Future of Genetic Information in Healthcare Information Assurance and Security

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ABSTRACT
The risks associated with the misuse and abuse of genetic information are high, as the exploitation of an individual’s genetic information represents the ultimate example of identity theft. Hence, as the frontline of defense, information assurance and security (IAS) practitioners must be intimately familiar with the multidimensional aspects surrounding the use of genetic information in healthcare. To achieve that aim, this chapter addresses the ethical, privacy, economic, and legal aspects of the future uses of genetic information in healthcare and discusses the impact of these uses on IAS. The reader gains an effective ethical framework in which to understand and evaluate the competing demands placed upon the IAS practitioners by the transformative utility of genomics.

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INTRODUCTION

Biotechnology and its related applications are advancing rapidly. As readers in the field of information assurance and security, you may wonder what biotechnology advancements have to do with information security. The intersection is clearly seen when one considers the fact that the human genome is made up of over 3 billion bits of information, where these bits are nucleotide base pairs. Viewed in this context, the human genome as information is slightly different in nature from other forms of personal information, such as a social security number, a credit card number, your name, your address, and so on. The difference is as follows. If an individual’s social security or credit card number is compromised, she can get a new one – albeit not without some effort and cost. In fact, one can even get a new name. This is not the case with your genome. In this case, you are your information and always will be. Furthermore, the utility of this information could extend beyond your life. Your children and grandchildren are derived from your genome; they are information derivatives.

As such, consideration of the use and potential misuse of genetic information seems highly relevant to information assurance and security. We believe that IAS practitioners should be aware of the evolution of biotechnology and the consequent implications for the use of genetic information. Toward this end, this chapter discusses a particular area, known as pharmacogenomics, which is overviewed in the next section, and considers some of the ethical, privacy, economic, and legal aspects of the future uses of genetic and pharmacogenomic information in healthcare.

We begin with an overview of pharmacogenomics so that readers have a basic grounding. Next this chapter discusses the promise of technological innovation so that readers understand how advances are perceived as beneficial to society. Then we analyze ethics and genetic information, with a concentrated focus on ethics and pharmacogenomics. The analysis serves as a model demonstrating how critical ethical analysis of past innovations can serve to reveal whether or not there really is anything “ethically new” here. As you’ll see, we conclude that with regard to pharmacogenomics, yes, there are a few novel challenges for consideration. Given that many ethical challenges are linked to public policy and social norms, we turn to discussion of how existing laws and social norms may or may not address/influence some of these challenges. Finally, we end by discussing implications for models of information assurance and security, bringing full circle the ramifications of biotechnology to information assurance and security.

Before we proceed to a discussion of background topics, let us highlight relevant information assurance and security concepts as these are some of the criteria by which we later evaluate the pertinent ethical issues that arise from the use of genetic information in healthcare. According to Bishop (2002) as well as Whitman and Mattord (2005), the fundamental IAS concepts include confidentiality (which includes privacy), integrity, availability, and evidence of trustworthiness. Confidentiality is the concealment of information or resources, and access control mechanisms help to enable confidentiality (Bishop, 2002); generally speaking, confidentiality has a close relationship with privacy (Whitman & Mattord, 2005). Privacy is a complex concept with many nuanced definitions (Schoeman, 1984); for our purposes, we delimit the definition of privacy to one’s independent control over the public dissemination of one’s personal information. Integrity, according to Bishop, refers to the trustworthiness of data or resources, and is usually operationalized in terms of preventing improper or unauthorized change. As such, integrity entails mechanisms that prevent modification or detection of the integrity of the data (Bishop, 2002). In tandem with confidentiality and integrity comes availability, which concerns access to the desired information or resources (Bishop, 2002); a classic example of not providing avail-
ability is a denial of service attack (Bishop, 2002). Lastly, evidence of trustworthiness concerns the assurance that a piece of information meets the security requirements expected by the user of the information, and as the phrase suggests, evidence must exist that supports this trust (Bishop, 2002). Together, these concepts (confidentiality, integrity, availability, and evidence of trustworthiness) form the basis of evaluation for the IAS professional as she or he encounters the ethical issues addressed later in this chapter.

**BACKGROUND OF PHARMACOGENOMICS**

Pharmacogenomics is the utilization of genomic markers – pieces of information used to identify and track genetic characteristics – to personalize prescription drug dosing and falls into the broader area of “personalized medicine”. To elaborate, we need to provide a brief background in genetics – it’s our aim to do this in a manner that is understandable by readers not steeped in a biology/genetics background.

The human genome, which is made up of over 3 billion bits of information (nucleotide base pairs), contains approximately 24,000 gene sequences. Furthermore, the human genome harbors over 1 million single nucleotide polymorphisms (SNPs). A SNP is a known location in the genome where a single base differs within the population. Therefore, SNPs are similar to genetic “mutations”. The difference between a mutation and a SNP is that a mutation is known to be causal to a specific disease or disorder, whereas SNPs are simply seen as benign genomic differences among individuals. It is important to note that mutations and SNPs are not the same type of information when we classify information by its use. Currently, we are not using SNPs to predict a disease or disorder. Rather, the advances in biotechnology are exploring how SNPs can be used to predict and improve the outcomes of medicinal treatment, which we discuss in more detail later. But that is current day. Research is also underway that examines the role (if any) that certain SNPs play in the predisposition of specific diseases. As the medical community begins to derive predictive information about the future health of a patient from their DNA sample, the power of the utilization of genomic markers, as well as the associated liabilities, come into focus.

**THE PROMISE OF PHARMACOGENOMICS**

Health is essential to human flourishing. We all know first-hand the importance of health to quality of life; without health, matters of life, liberty, and pursuit of happiness seem less relevant. To understand why pharmacogenomic advances are being pursued, we need to take a closer look at how pharmacogenomics promises to contribute to human and social welfare.

SNPs associated with the genes that play a role in drug metabolism or drug action can be utilized to identify patients that may be at risk of experiencing an adverse drug reaction (ADR) when taking a specific medication. Adverse drug reactions can range from being relatively mild (e.g., headache), which sometimes causes patients to discontinue taking a needed medication (i.e., decreased compliance) to very serious and life threatening. Thus, one of the value propositions of this form of personalized medicine focuses on the potential it has to reduce the risk of adverse drug reactions in the population, increase dosing compliance and efficacy in the population. The implication is that by reducing risk of adverse drug reactions and increasing dosing compliance and efficacy, we will ultimately reduce healthcare costs. In other words, there is not only a quality of life motivation, there are economic and “healthcare outcome” benefits to utilizing a patient’s DNA sample to support personalized prescription drug dosing.
The cost of ADRs is significant. According to a 1997 study (Classen, Pestotnik, & Evans), more than 770,000 patients die or sustain serious injury every year in hospitals from adverse drug reactions. It is likely higher now. Another study (Bates, Spell, and Cullen, 1997) found these ADRs were estimated to cost individual hospitals approximately $5.6 million per year and in terms of total health care dollars, ADRs were estimated to cost the U.S. health care system between $1.5 and $5.4 billion per year. While exact rates of ADRs are difficult to calculate, in 2000 it was estimated that adverse drug reactions accounted for 2% to 7% of hospital admissions (Thomas, Studdert, Burstin, Orev, Zeena, & Williams, 2000).

It is believed that patients who have experienced an ADR have longer and more costly hospital stays than those who do not. In a study funded by the Agency for Health Care Quality (AHRQ), it was found that patients with a serious adverse drug reaction had an average additional length of stay of 20 days ($38,007 in costs) and patients suffering from less severe ADRs had an average stay of 13 days ($22,474 in costs). These compare to patients with no ADR who had an average length of stay of 5 days and $6,320 in costs (Evans, Pestotnik, & Classen, 1992). Classen et al. (1997) found that patients who experienced an ADR were hospitalized on average one to five days longer than patients who did not, with an additional cost to the hospital of approximately $9,000. Bates et al. (1997) found on average an increase length of stay of 4.6 days and up to $4,680 in additional costs for patients with adverse drug reactions. Despite differences, the findings across all studies support the claim that adverse drug reactions are an area where medical costs could be reduced. This opportunity first received major attention with the release of the report by the Institute of Medicine entitled To Err is Human: Building a Safer Health System. This report provided an in depth analysis into medication errors with the goal of building a better and safer health care system that limits mistakes and improves patient outcomes (Kohn, Corrigan, & Donald, 2000), and has been one catalyst for the advancements in pharmacogenomics.

An exemplary case study concerning the potential impact of pharmacogenomics on ADRs concerns the anticoagulant Warfarin. Warfarin is an anticoagulant (a blood thinner). This drug was initially put on the market as a pesticide – to kill mice and rats for example – and is still used for this purpose. In the early 1950s it was approved for use in humans given its effectiveness in preventing abnormal formation and migration of blood clots. Today, as many as 2 million patients a year may begin therapy with warfarin (Wu & Fuhlbrigge, 2009).

Treatment with warfarin is not without shortcomings. Many patients take weeks if not months to become stabilized on warfarin therapy. Research has found that warfarin was the third most common drug to cause a hospital admission due to an adverse drug reaction (Pirmohamed, James & Meaken, 2006). Another study found that bleeding complications associated with warfarin therapy were responsible for 29,000 emergency department visits per year (Wysowski, Nourjah, & Swartz, 2007). While the drug product itself is extremely inexpensive to purchase, the monitoring and follow-up can be very expensive.

For patients with two well known SNPs1, there is a significantly elevated risk of inadvertent overdosing when the “normal” dose is administered. These patients have a decreased drug metabolism rate, resulting in drug levels in the body that exceed safe limits and a serious adverse drug reaction. In August of 2007, the U.S. Food and Drug Administration (FDA) updated their recommendations when prescribing warfarin to include consideration of genetic testing. The FDA product labeling therefore recommends SNP2 screening for patients upon initiation of warfarin therapy.

A report by the AEI-Brookings Joint Center for Regulatory Studies suggested that testing for polymorphisms3 would decrease health care spending in the U.S. by $1.1 billion annually.
(Wu & Fuhlbrigge, 2009). Another report by economists at the FDA estimated that such testing before the initiation of warfarin therapy could save the U.S. healthcare system $1.1 billion annually, avoid 85,000 serious bleeding episodes, and prevent 17,000 strokes (Hughes & Pirmohamed, 2007). The report further suggested that 5% of all thromboembolic strokes (that is, a stroke caused by a blood clot in the brain) could be prevented by this type of genetic testing.

These data clearly suggest that pharmacogenomic testing before the initiation of warfarin therapy has the potential to provide substantial cost savings and improved patient outcomes.

Furthermore, there are many other medicinal drugs that will provide better and safer treatments if clinical genotyping is utilized to identify patients at higher risk of adverse drug reactions. The long term impact of personalized medicine on the therapeutics market will involve a greater diversity of medicinal drugs available to the healthcare community (reflecting the genetic diversity of the population), but will require genotype screening to insure a specific drug/dose is both safe and effective for an individual.

There are numerous potential advantages of obtaining genomic information through pharmacogenomic testing. However, there are also several questions that merit further deliberation, such as these. Will the public embrace pharmacogenomic testing or will there be backlash given concerns of privacy and discrimination? Will we find that SNPs can be used for disease and disorder prediction? If so, what might be the implications, advantages, and concerns? When? How? By whom? What is the potential for misuse of such information? Are existing laws and social norms sufficient to mitigate misuse? Are existing information assurance and security models robust enough to apply to genomic information? Clearly, this leaves a number of unknowns.

When challenged with new uncertainties, the question as to how move forward can be paramount. Frequently, moving forward requires careful consideration of past – a critical and analytical inventoring if you will. It is to this that we turn next.

ETHICS AND GENETIC INFORMATION

In the recent past, development of new biotechnologies utilizing genetic information, such as cloning of individual animals, the development of genetically modified organisms, or bio-enhancement utilizing nanotechnologies, has led to serious ethical concerns. These developments and subsequent concerns have given rise to the notion of “genetic exceptionalism” (Murray, 1997). As the phrase suggests, the key idea embodied in genetic exceptionalism is that genetic information is qualitatively different from other forms of health information. The predictive, personal, and familial nature of genetic information suggests that it has a unique status and should therefore be treated differently.

Advancements in biotechnology have led to the development and implementation of new genetic tests. The ethical problems have not been with use of genetic testing per se but, as mentioned earlier in this chapter, with the use and interpretation of the information obtained through genetic testing. Thus, as we discuss pharmacogenomic testing in the following section, keep in mind that we are referring to the information obtained through this particular type of testing.

Pharmacogenomics, a relatively new area in biotechnology, requires the development of new genetic testing. Given that past biotechnologies have been plagued with ethical concerns, contemporary pharmacogenomics likewise runs the risk of being so plagued. It would seem prudent, therefore, to take heed of the negative implications of the past and tread carefully when using the information derived from pharmacogenomic testing. Let us call this the “prudential argument” against pharmacogenomics.
What are the negative implications of such use? There are two common ways these implications may be morally evaluated. Either one may take a bottom-up approach, where individual cases lead to common ethical issues; or one may take a top-down approach, where ethical principles guide the evaluation of individual cases. The former is a type of inductive approach: in much the same way that we commonly expect the sun to rise tomorrow based on previous sunrises, so too do we expect similar moral outcomes from similar individual cases. The latter is a type of deductive approach: given the Law of Universal Gravitation for example, we are able to derive that if one drops a pen from her hand, then it will fall to the floor. Similarly, starting from ethical principles we can evaluate individual cases and decide whether they conform to those principles.

The incipiency of the field makes it difficult to utilize a bottom-up approach since there are not sufficiently relevant cases to evaluate. As such, our evaluation applies a top-down approach, utilizing a standard set of four ethical principles as defined by Beauchamp and Childress (2001). Evaluation of the prudential argument calls for us to determine whether the potential ethical issues arising with the development of pharmacogenomic testing and the use of information derived from this testing fulfill the moral requirements established by these four principles. Application of these four principles to the case of genetic testing for drug efficacy allows us to mark potential ethical hazards that can then be gone over with a finer-toothed ethical comb. We will first consider ethical issues with the development and implementation of genetic testing generally and then determine whether, and to what extent, pharmacogenomic faces these same issues.

Genomic Research and the Principle of Respect for Autonomy

According to Beauchamp and Childress (2001), the principle of respect for autonomy involves both negative and positive obligations (p. 64). They further explain that negative obligations require a “respectful attitude” (p. 63) that acknowledges “a person’s right to hold views, to make choices, and to take actions based on personal values and beliefs” (p. 63). And, positive obligations require “respectful action” understood as an obligation “to build up or maintain others’ capacities for autonomous choice while helping to allay fears in other conditions that destroys or disrupts their autonomous actions” (Beauchamp & Childress, p. 63). Given this principle, we can approach three major ethical issues regarding autonomy that appear in the literature: informed consent, privacy and confidentiality, and ownership of genetic information.

First, the debate around informed consent involves what information a researcher is obligated to provide to his or her human subjects concerning the term and conditions of the research project. Traditional models of informed consent are in place to protect the autonomous choice of the human subject. The subject is allowed to weigh costs and benefits of his or her own voluntary participation in the research project based on sufficient disclosure of information concerning that project. In providing sufficient information to his human subject, the researcher fulfills both negative and positive obligations: he has taken a respectful attitude toward his subject’s right to autonomous choice and has taken respectful actions to uphold and protect that autonomy. Genomic research, however, calls into question this model. Why? Let us consider the following general example. A genetic researcher wishes to verify a genetic link between risk for specific disease and a specific population of human subjects. To do so, he seeks informed consent from all the subjects of the group and completes the study. The results of this study prove his hypothesis: indeed, there is a correlation between the genetic variant in that population and the disease. With this result, the study population has increased to include not only all those participants who had
given consent, but all members of the population who share that genetic variant. The researcher has failed his obligations to respect the autonomy of the community at large since some members of that population could suffer a type of group-based harm. Genomic research might also face this problem of a lack of community consent, understood as the consent of every individual affected by a study and not only each participant in the study.

Second, pharmacogenomic research, like all genetic research, faces problems of privacy and confidentiality: release of genetic information from pharmacogenomic research can lead to increases in psychological, economic, and social risk. There are abundant examples in the literature regarding psychological risk tied to the release of genetic information. If within a family unit the parents discover that they carry a genetic mutation linked to a specific disease (i.e., BRCA1, BRCA2 to breast cancer), the psychological well-being of the entire family including the children is negatively affected (Franklin, 2008). Moreover, the release of genetic information can lead to increased economic risk. For instance, a study published in 1996 based on 332 families affected by genetic diseases found that 22% of the subjects had been refused by a medical insurance corporation and 13% had been fired for infection risk (Lapham, Kozma & Weiss, 1996). Certainly, legislation passed by the United States Congress and signed into law in 2008, the Genetic Information Non-discrimination Act (GINA, 2008), seeks to avoid these economic perils. Pharmacogenomic testing, however, may not be covered by GINA. GINA does not require that an insurance corporation, for example, cover a particular test or treatment. If pharmacogenomic testing proves that an individual has a difficult-to-treat genotype, they have no obligation to cover the necessary treatment. Hence economic risks based on this testing may be very real indeed. Moreover, we share Billing’s idea that “legislation is not a panacea for genetic discrimination” (Billings, 2008, p. 806) in much the same way that legislation regarding previous forms of discrimination have ended neither racism nor sexism. Likewise, disclosure of information derived from pharmacogenomic tests could easily lead to increased social risk; i.e., the stigmatization of a population based on genetic difference.

Third, genetic researchers must be concerned with the ownership of genetic information. Should biotech companies be allowed to build and maintain large biobanks of genetic information? Who ultimately owns this information: the donor of the biological sample or the researcher analyzing that sample? This issue was brought to the public’s attention with the case of John Moore in 1990 (Skloot, 2006). Moore, while being treated for a rare form of cancer, had his spleen removed. Researchers found what Eric Meslin (2008) has called an “incredibly cool cell line believed to be predictive of his genetically-mediated cancer”, which they cloned and patented, without informing Moore. Interestingly, Moore lost the pending lawsuit concerning ownership of the patented cell line: the California Supreme Court ruled that an individual does not own the biological material of his or her own body removed and manipulated by researchers. However, in a following obiter dicta, Justice Mosk suggested that while the property rights decision was just, Moore may have legitimately argued that the researchers failed an obligation to protect his autonomy by not seeking his fully informed consent (Moore v. Regents of University of California 1990). Moore does not own biological or genetic products derived from his own biological or genetic material, but does have the right to be fully informed about the collection and use of that material. Pharmacogenomic testing will have to face these issues of ownership of genetic information in much the same way. Access to genomic information must be mediated against risk: financial interests should not over-ride the researcher’s moral and legal obligations to full disclosure both concerning the scope of the research project and the researcher’s conflicts of interest.
On the topic of autonomy, the obvious concern for IAS professionals involves patients’ confidentiality and privacy. Given our working definition of privacy that characterizes privacy as one’s independent control over the public dissemination of one’s personal information, one can see that independent control is based on the type of autonomy that we describe in this section. In the form of one’s access to her or his own genetic information, availability is another consideration in this context for IAS professionals as is assurance; in this case, assurance concerns the trust that the patients have in the capacity of the underlying information system to maintain their ownership of their own genetic information. This is akin to the concern raised with electronic health records (EHRs) where the lack of trust in the security of the data may lead patients to conceal sensitive information (Layman, 2008).

Genomic Research and the Principles of Nonmaleficence and Beneficence

In much the same way that the principle of autonomy comprised both positive and negative obligations, so too, may we make the distinction between the positive principle of beneficence and the negative principle of nonmaleficence. However, just because a principle is negative does not likewise imply that the obligation it outputs should be fulfilled in a passive way. Nonmaleficence is the obligation “not to inflict evil or harm” (Beauchamp & Childress, 2001, p. 115). This is a negative principle that moves beyond a mere attitude of non-interference: it obligates us not to perform some action; i.e., it prohibits the actions of theft, of disablement, or of killing.

However, this is only one side of our obligations. As Beauchamp and Childress argue, “[m]orality requires not only that we treat persons autonomously and refrain from harming them, but also that we contribute to their welfare” (Beauchamp and Childress, 2001, p. 165). So, contributing to one’s welfare falls under the principle of beneficence. This is a positive principle that requires us to prevent or remove evil or harm and promote good: we ought to proscribe benefits, protect interests, and promote welfare (Beauchamp and Childress, 2001, p. 114).

Genetic tests generally are tools utilized to assess the predisposition for some medical condition. As such, they per se cannot inflict harm. Recall the genetic test regarding BRCA1/BRCA2. It is not the information given by the test that causes psychological harm per se; rather, it is the limitations that that information imposes on your autonomous choice that causes harm. Apart from these psychological, economic, and social risks of harm outlined above, it would seem that whenever a genetic test is applied with no malicious intention it could not be done maleficently. However, this is only one side of the question. On the other side, we must ask whether genetic tests promote the welfare of the test recipient. Health is a good that promotes welfare and so whenever a genetic test is applied to increase health, it promotes welfare. Therefore, whenever genetic tests are applied to increase health, they are applied beneficently.

The concern related to assurance that we raise in the preceding section applies here in this section in a slightly different manner. Specifically, the lack of trust that the patients have in the capacity of the underlying information system to maintain their ownership of their own genetic information may lead patients to conceal sensitive information, and this concealment may have a negative impact, not only on their health, but on advances in biotechnology that contribute to collective welfare. Conversely, providing evidence of the trustworthiness of the system – which includes ensuring the integrity of the data – may positively impact patients’ health by leading them to adopt and use the system, which in turn has implications for the collective.
Genomic Research and the Principle of Justice

There exist a wide variety of theories of justice—egalitarian, utilitarian, communitarian, libertarian, et cetera. As Beauchamp and Childress have argued, there is “no single theory of justice or system of distributing health care [that] is necessary or sufficient for constructive reflection on health policy” (2001, p. 272). However, all theories of justice share as a minimal requirement Aristotle’s principle of formal justice: “treat like cases as like” (Aristotle, trans. 1984a, 1131a10-b15 & trans. 1984b, 1280 a8-15). Aristotle’s statement implies that equals ought to be treated equally and unequal’s ought to be treated unequally; however, it is a basic or formal principle in that it does not describe how this equality is to be determined. Each contemporary theory of justice that builds on Aristotle’s minimal formal principle can play a role in our moral decision-making. It will suffice here to lay out several potential challenges of justice within the narrow scope of the formal principle—solutions to those principles are contingent on the more robust and particular theory of justice one accepts. In a biomedical context, issues of justice are commonly issues of fair and equitable distribution of resources.

Genomic testing faces several challenges in terms of justice. By delineating genetic differences in the population, genomic testing could support various forms of discrimination, each of which affects the equitable distribution of resources.7

First, the development of genomic testing brings with it risk of additional forms of discrimination. As we have argued, according to any theory of justice discrimination amongst equals is a moral wrong. Any third-party access to genetic information, including SNP references, has potential to lead to discrimination by a host of agents. Insurance companies, for instance, might increase rates given certain information linking a person’s genetic variants to increased risk of disease or disorder. While federal legislation including the GINA of 2008 has taken steps to prevent just this sort of discrimination, it is still unclear whether further legislation is required to seal loopholes created by this new pharmacogenomic mapping technique. Additionally, discrimination by the potential connection of SNPs to race, ethnicity, or socio-economic class may lead to new forms of stereotypes based on new minority populations. If pharmacogenomic research provides evidence for correlation between a particular SNP and a particular drug given a particular set of research subjects, the researcher must consider the risk of discriminating against other individuals outside of the research group who might also benefit from the drug (Decamp & Buchanan, 2008, p. 544).

Second, if the future development of pharmaceuticals is driven by increases in the efficiency of some medical treatment for a given genetic population, it is easily foreseeable that whenever the population is sufficiently small in size or poor in resources, the economic incentive might not be available to drive drug research and production. Thus, some genotypes will be “orphaned.” It seems that pharmacogenomic testing may lead to discrimination against any orphaned genotypes identified by this technology (Decamp & Buchanan, 2008, p. 541).

Clearly, genomic testing faces ethical dilemmas in terms of justice. Ultimately however, these questions of justice must be weighed pragmatically against increases of risk and cost, and threats against autonomy.

On the topic of justice, availability is the most important consideration in this context for IAS professionals. Layman (2008) raises the concern that EHRs fail to provide increased access for disadvantaged persons, and without access to their own genetic information, the same fate may befall disadvantaged persons in the area of pharmacogenomics. On the other hand, the possibility of discriminatory activities must lead
the IAS professional to careful consideration of the ethical dimensions of providing such access.

**The Ethical Implications of Pharmacogenomics**

The ethical concerns presented in the sections above lend credence to the prudential argument: given both the continuity between pharmacogenomic testing and other types of biotechnologies and the ethical issues plaguing these other biotechnologies, we should be cautious in the development of pharmacogenomic testing. However, the soundness of this argument is based on a hidden premise; namely, that there is no significant difference between pharmacogenomic testing and other genetic testing. The truth of this premise can be called into question. A central difference is that pharmacogenomic testing, unlike other genetic testing, is not necessarily or even primarily associated with disease information/prediction but instead merely seeks out efficiency of treatment. In fact, Roses and others have noted that “[e]thical, legal, and social implications for ‘genetic tests’ of single-gene mutational diseases should not automatically be assumed for other non-disease-specific applications simply because they are labeled imprecisely as ‘genetic tests’” (Roses, 2000, p. 858). Pharmacogenomic tests are unique to genetic tests specifically because they do not predict disease. So perhaps the prudential argument fails: pharmacogenomic testing is sufficiently different that we can proceed unfettered.

Or can we? We should not automatically assume there are no possibilities to link information to disease. Some researchers maintain that some possibility remains that a genetic marker made available by pharmacogenomic testing could be linked to some disease predisposition, either environmentally or genetically mediated (Lindpaintner, 2001, p. 26; see also Lindpaintner, 2003; Schulte, Lomax, Ward, & Colligan, 1999).

We are left with the grounding that ethically-speaking, pharmacogenomic testing still seems to stand apart from other types of genetic testing, assuming we do not use genetic markers to predict disease. How then are we to define an ethical approach to pharmacogenomic research in the face of uncertainty? Let us consider how the unique status of pharmacogenomic testing affects the ethical issues we described above.

First, it has been suggested that pharmacogenomic testing leads to three major issues regarding the principle of respect for autonomy. Do these issues still hold if we consider pharmacogenomic testing a unique type of genomic testing? The first of these issues regarding autonomy, the problem of informed consent, still holds; however, it holds not only for pharmacogenomic research and genetic research but also for all research findings associated with a group. So the uniqueness of pharmacogenomic testing as a genomic test does not absolve the risk of infringing on the autonomy of all the members of the population who share some genetic variant. The second of these issues, related to privacy and confidentiality, greatly reduces the risk of psychological, economic, and social harms prevalent in other genetic testing precisely because pharmacogenomic testing does not predict disease. The psychological harm mentioned above is related to disease prediction. Merely determining efficient drug dosage does not bring with it these harms to the same degree. However, some economic and social risks could still persist. Consider that *ceteris paribus*, for an equally efficient treatment of some disease, a pharmacogenomic test reveals that an individual must take twice the dosage of some other individual. Here exists an economic risk: if the former individual does not have the economic means to afford the treatment, his choice of treatment will be limited; thus, his own autonomy will be limited as well. The third of these issues is related to biobanking. It seems hard to believe that the uniqueness of pharmacogenomic testing will remove all concern regarding
biobanking. Even given this new premise, there will still be issues regarding storage, manipulation, and ownership of genomic information. For the ethical practice of pharmacogenomic testing, significant consideration of past informed consent failures is paramount. Despite pharmacogenomic testing not linking genetic information to disease and thereby avoiding the more significant harms of other genetic testing, it is nonetheless crucial to promote and respect the autonomy of the individual research subject.

Second, pharmacogenomic testing seems to fulfill the moral requirements of both of the principles of nonmaleficence and beneficence. This medical technique was developed specifically to prevent harm. By determining a link between specific single nucleotide polymorphisms and the level of absorption of various compounds introduced in the body, this research aims to prevent and reduce drug-adverse reactions: a serious problem with contemporary pharmacology (Kohn et al., 2000; Neil & Craigie, 2004). Moreover, pharmacogenomic testing represents a potential major step forward in personalized medicine: not merely by ending one-size-fits-all medicine but by finding the maximally efficient and effective treatment dosage for a particular disease of a particular individual. In so doing, this medical technique supports the removal of harms by fitting the proper treatment to the individual: not only can the proper dosage of a particular drug avoid killing or harming the patient, but also can provide a sufficient amount of drug as an effective treatment. Overall, pharmacogenomic testing has potential to promote good by supporting the health of the individual. Since the health of individual leads to the general health of that individual’s community, pharmacogenomic testing can support the overall health of the community.

Third, pharmacogenomic testing faces ethical challenges regarding discrimination and problems of orphan genotypes. These problems persist regardless of the unique status of pharmacogenomic testing among other genetic tests. Having considered the ethical implications of pharmacogenomics, it is now helpful to evaluate the current state of medical practice and existing laws as they concern genetic information and its use, and in doing so, to understand better the interplay between the ethical and legal dimensions of the use of genetic and pharmacogenomic information in healthcare. We do so in the following section.

EXISTING LAWS

The Edwin Smith Papyrus, which dates to the sixteenth century BC (Wilkins, 1992), is the earliest known recording of patient information and histories. The significance for us today is the recognition that medical records have been a common practice in the medical profession for centuries. Given advances in technology, i.e., the advent of internet technologies, the emergence of mobile devices, and standards efforts such as Health Level Seven (HL7), health records are no longer only housed in paper-based form in storage cabinets in physicians’ offices. Electronic health records are a common practice in most medical operations.

Electronic health records are viewed as having the potential to increase access to health care, improve the quality of care, and possibly decrease costs (Layman, 2008) – all important social values. While these are desirable outcomes, Layman (2008) points out that EHRs have not increased access for disadvantaged persons, improved the accuracy of records, nor positively impacted productivity. Furthermore, Layman (2008) discusses a multitude of other ethical issues concerning EHRs. Specifically, there may be a negative impact on a patient’s autonomy when their health data are shared without their permission. Moreover, a “lack of confidence in the security of health data may induce patients to conceal sensitive information,” and as a result, “their treatment may be compromised” (Layman, 2008). In response
to concerns such as these, we have seen growth in legislation. One primary piece of legislation pertinent to electronic health records is the Health Information Portability and Accountability Act (HIPAA, 1996) – The goals of the HIPAA focus on five primary areas: individual control of one’s medical information, boundaries on the use of medical information, privacy accountability, balance between the use of medical information for the public good at the expense of an individual’s privacy, and the security of medical information (Whitman & Mattord, 2005). In addition to HIPAA, to date 32 states have enacted genetic privacy laws. These laws aim to protect genetic information beyond the measures taken in other laws such as HIPAA. That we need special laws to offer such protection for genetic information reflects a substantial shift in the public’s awareness of their privacy needs as they relate to their genetic information. In essence, these laws suggest that genetic information is different than other information such as bank accounts and Social Security Numbers.

The state genetic privacy laws for the most part place restrictions on certain entities, such as insurers or employers, from carrying out given actions without the individual’s consent. The actions that are restricted range as follows: performing or requiring a genetic test; obtaining or accessing genetic information; retaining genetic information; and disclosing genetic information. There is variation among the state laws. For example, 12 states require consent to perform or require a genetic test, 7 require consent to obtain or access genetic information, 8 require consent to retain genetic information, and 27 require consent to disclose genetic information. Five of the state laws specifically define genetic information as personal property and one includes DNA samples as personal property. Other elements in some of the genetic privacy laws are the provision for the individual to have personal access to his/her genetic information and a provision for penalties in the case of privacy violation. Clearly, there are divergences; 64% of the states have laws and these laws are notably varied. Detailed information on the criteria by state is available at the National Conference of State Legislatures website (www.ncsl.org). For our purposes, the important point is not how these laws differ among states, but that they do. These differences clearly demonstrate the differing views on socially accepted practice.

As discussed earlier, in addition to privacy issues, genetic information has implications for discrimination. To address this, there are a number of state laws that prohibit the use of genetic information when providing health insurance and separate state laws that pertain to the use of genetic information in employment decisions. Currently 48 states have laws that address genetics and health insurance anti-discrimination by placing restrictions on health insurers. In some states, the law pertains to individual insurance policies, in other states it pertains to group insurance policies, or both. These laws do not apply to employer-sponsored health insurance, which is under the purview of federal legislation. The types of restrictions found in these laws are: prohibit the use of genetic information to determine eligibility for insurance; prohibit the requirement of genetic testing in order to obtain insurance; prohibit the use of genetic information for risk classification and premium setting, and; prohibit the insurer from disclosing the genetic information without prior consent from the insured. Some states have only one restriction, where others include all four. Furthermore, some states have exceptions, such as allowing the use of genetic information for setting premiums when it benefits the individual. Summary detail can be found on the National Conference of State Legislatures website (www.ncsl.org).

To address employment discrimination, thirty-four states have laws that prohibit the use of genetic information in employment decisions. These laws make it illegal to discriminate when making employment decisions (hiring, firing, and terms or conditions of employment) based on
the results of genetic information. The types of restrictions are prohibition from: requesting genetic information; requiring genetic information; performing a genetic test, and; obtaining genetic information from a genetic test. Not surprisingly, the prohibitions vary among states and detail can be found at www.ncsl.org.

At the federal level, several forces converged to lead to the passage of the aforementioned GINA in 2008. This act prohibits the use of genetic information in both insurance and employment decisions. GINA specifically addresses genetic information that is not sufficiently covered by HIPAA and seeks to address gaps and inconsistencies in the state laws. GINA provides a baseline level of protection to all U.S. citizens regardless of which state they reside in. By addressing the threat of discriminatory practices, GINA aims to assure patients that their genetic information is safe. This assurance is needed to increase the number of citizens who participate in genetic testing, as it is through such testing that the research community gathers the needed biomedical data to better understand and ultimately advance healthcare.

Critics of GINA note several outstanding concerns. First, GINA fails to rectify inconsistencies between state laws, leaving multistate entities responsible for complying with different regulations in each state. Second, GINA is overly broad leaving considerable room for interpretation. Third, GINA fails to prohibit insurers from using genetic information when establishing life, long-term care, and disability insurance; therefore, it does not go far enough in preventing discriminatory practices. And last, critics contend that GINA fails to allow us to use genetic information to its fullest potential by not requiring insurers to cover preventive care when a genetic test indicates that such care could prevent or minimize a health risk.

While it is common for societies to utilize public policy to address macroethical issues, it is prudent to keep in mind that laws, per se, cannot address all of the ethical issues society encounters. Science and technology forge ahead in a state of uncertainty. While today we do not think that SNPs can be used for disease prediction, we do not know that for certain. It also behooves us to be mindful that policy works at a much slower rate than technological innovation. Such implications are important for professionals where, in the face of uncertainty, complying with the law is a minimum expectation and acting in the best interests of society an ongoing aspiration. So, where does this leave us? What are the implications for information assurance and security?

**IMPLICATIONS FOR INFORMATION ASSURANCE AND SECURITY**

Probably the most profound implication for information assurance and security is seen by again focusing on the nature of genetic information, present and future. In reflecting on relevant laws, such as HIPAA and the varying genetic information laws, we can see that formal definitions of information have been enacted by legislative bodies. However, our working definitions of information are much more elusive, which suggests that the true nature of information is as a “moving target”. Information is, and will continue to be, evolving. As evidence we offer this chapter as an assertion; biotechnological advancements are requiring students and practitioners in information assurance and security to expand their concepts and definitions of information to encompass the data derived from the ever-growing list of genetic tests.

And what of this type of information? What properties does it possess that perhaps characterize it in a manner that determines how it is to be assured and secured? According to researchers, genetic/genomic test information has unique characteristics that must be considered when determining appropriate protection (McGuire, Fisher, Cusenza, Hudson, Rothstein, McGraw, Matteson, Glaser, & Henley, 2008). These characteristics are as follows. Genetic information is especially unique—excepting identical twins, each individual
has a unique genetic code. Genetic information is immutable—an individual’s inherited information does not and, for the most part, cannot change. Genetic information has predictive capability and familial network effects—such information can be used to make predictions about oneself and one’s family spanning generations. McGuire et al., (2008) also advise that given the relative novelty of genetic testing and genetic information, treating this field holistically is advisable. As such, they note several relevant, contextual factors. First, we have a history of misuse of genetic information to promote eugenics initiatives and obtain information about individuals for purposes of discrimination. Second, public opinions about the role and use of genetic information vary widely. Third, the technology is changing rapidly which exacerbates fear of further misuse and make public awareness even more challenging. And fourth, genetic information is getting increasingly easier to procure. Together, the characteristics of the information coupled with the context, highlights the need for models of confidentiality, integrity, availability, and evidence of trustworthiness that consider these relevant characteristics in a holistic manner that includes the ethical areas that we discuss earlier: autonomy, nonmaleficence/beneficence, and justice.

On the topic of autonomy, the obvious concern for IAS professionals involves patients’ confidentiality and privacy. Since our working definition of privacy characterizes it as one’s independent control over the public dissemination of one’s personal information, it becomes clear that independent control is based on the type of autonomy that we describe in this section. In the form of one’s access to her or his own genetic information, availability is another consideration in this context for IAS professionals as is assurance. In this case, assurance concerns the trust that the patients have in the capacity of the underlying information system to maintain their ownership of their own genetic information. This is akin to the concern raised with EHRs where the lack of trust in the security of the data may lead patients to conceal sensitive information.

The concern related to assurance that we raise in the preceding paragraph applies here in a slightly different manner. Specifically, the lack of trust that the patients have in the capacity of the underlying information system to maintain their ownership of their own genetic information may lead patients to conceal sensitive information, and this concealment may have a negative impact on their health. Conversely, providing evidence of the trustworthiness of the system—which includes ensuring the integrity of the data—may positively impact patients’ health by leading them to adopt and use the system.

On the topic of justice, availability is the most important consideration in this context for IAS professionals. Layman (2008) raises the concern that EHRs fail to provide increased access for disadvantaged persons, and without access to their own genetic information, the same fate may befall disadvantaged persons in the area of pharmacogenomics. On the other hand, the possibility of discriminatory activities must lead the IAS professional to careful consideration of the ethical dimensions of providing such access.

CONCLUSION

We might reasonably conclude that there are significant differences between pharmacogenomic tests and other types of genetic testing. While other genomic tests are developed to predict disease, bringing with them a host of difficult moral quandaries, pharmacogenomic tests are developed to maximize drug efficacy. In so doing, pharmacogenomic testing attains a unique status among types of genomic tests and minimizes potential ethical risks involving the privacy of genetic information, the autonomy of the individual, and the just distribution of health resources related to these tests.
Those remaining risks, outlined above, must be weighed against the potential and actual benefits of pharmacogenomic research. Pharmacogenomics as an essential part of personalized medicine is an increasingly attractive target for the future of medical practice. Steps forward demand a pragmatic prudence that will allow researchers and research subjects to evaluate risk and weigh benefits throughout development and implementation.

The future of pharmacogenomic research success depends on a proactive approach to the careful analysis of potential ethical issues. Despite this minimization of the ethical risks inherent in other types of genomic testing, there remains potential for increased risk associated, not with the development of pharmacogenomic testing, but with its implementation. Continuing to think through potential issues with the implementation of this type of tests will promote not only the efficacy of pharmacogenomic research but also the safety of its development.

In fact, the implementation of pharmacogenomic testing will require the services of IAS practitioners, as the genetic and drug data that intersect in pharmacogenomics require an information system that ensures privacy and security (Kane et al., 2008). Thus, these practitioners will have no recourse but to encounter the ethical dilemmas addressed in this chapter. In keeping with the notion that acknowledgment of the problem is a critical early step in any problem solving exercise, we have endeavored to raise the reader’s awareness so that she, as an expert in the IAS domain, will be equipped to ask the correct questions and to raise the appropriate concerns.

Fundamental to this awareness is, first, an acknowledgment of the possibility of genetic exceptionalism and, second, recognition of the irrevocable nature of losing one’s genetic information. Furthermore, the IAS expert must have an understanding that the acknowledged possibility of genetic exceptionalism dictates a heightened need for ethical behavior. Questions surrounding ownership, nonmaleficence/beneficence, access, discrimination, and biobanking remain; and, these questions may grow more onerous as the science behind pharmacogenomics evolves. So too will the science behind disease prediction evolve, bringing its own, more troubling ethical issues and threatening to create, collaterally, a turbid perspective on the ethics of pharmacogenomics.

As the protector and purveyor of assured genetic information, IAS practitioners must be ready to inform the debate and to formulate ethical responses as they encounter the misuses and abuses of genetic information.

REFERENCES


Moore v. Regents of University of California. 51 Cal.3d 120 (Supreme Court of California 1990).


ENDNOTES

1 Warfarin is predominantly metabolized by the oxidative enzyme “CYP2C9” (Aithal et al., 1998) and pharmacologically inhibits vitamin K epoxide reductase complex 1 (VKORC), which prevent the blood clotting cascade from forming clots (Lee, 2005). There are two SNPs in CYP2C9 that have a reduced capability for metabolizing warfarin, with 11% and 7% frequency in the Caucasian population for SNPs CYP2C9*2 and CYP2C9*3, respectively. Patients who are homozygous for these variant alleles (i.e. patients have two variant copies of the 2C9 gene) experience a 65% decrease in drug clearance rate and therefore have elevated plasma levels of the drug.

2 In particular, screening for CYP2C9 and VKORC

3 In CYP2C9 and VKORC1

4 There are stricter and more moderate views of the requirements for informed consent. Compare, for instance, Jay Katz’s strict view (Katz, 2002) with Childress and Beauchamp, 2001.

5 Group-based harms are not concerns unique to pharmacogenetic or even to genetic research more generally (Decamp & Buchanan, 2007, p. 547).

6 An example commonly given in the literature is the Ashkenazi Jewish population. See Decamp and Buchanan, 2007, p. 544.

7 As a general concern that is not immediately relevant to IAS professionals, genomic testing faces the issue of access; namely, how do we most justly distribute access to a particular test? The obvious obstacle to just access to genetic testing is the price of the test. For instance, there is a patent on BRCA1 and BRCA2 testing held by Myriad Genetic Laboratories. Before cutting a deal with NIH, Myriad was charging up to $2580 for patient-requested analysis (Hollon, 2000, p. 610). Individuals who cannot afford that test or whose insurance companies will not cover that expense have no access to the BRCA testing. One might think that the mean price of these tests will decrease with the continued research and development of genetic testing; however, patenting and insurance obstacles will remain. Apart from the obvious economic questions of access, geographical questions of access must also be taken into consideration. Even if increases in availability of the test itself continue to develop, translation of that information will continue to require genetic counseling which may not be as equally distributed geographically.

8 As a general consideration beyond the realm of IAS, we ought to consider this question of access both in terms of future and present access. Consider the scenario of the future of pharmacogenomic testing: a pharmaceutical corporation develops a new drug to combat some disease. It is likely that, given technological innovation of pharmacogenomic testing, this corporation will develop and release such a test in tandem with the drug. Keeping the cost of this test within a range accessible to everyone who purchases the drug will help ensure that the drug itself remains on the market, avoiding the past problems of inefficiency and adverse reactions. Such
adverse reactions would cause the drug to be pulled from the market, imposing significant cost to the corporation. Thus in this future scenario, it seems that there is no question of access to the test per se, apart from questions of access (economic, geographical, etc) to the drug. However, the present status of pharmacogenomic testing is quite different from this utopian vision of the future. In the present, pharmacogenomic researchers continue to seek to develop tests for drugs currently available in trial or on the market. Assume that one such researcher has success. In this case, too, it seems that there would no problem of access to the test per se: it would be to the economic benefit of the corporation to make that test as widely available as possible, to prevent risk of adverse reaction or inefficient absorption. In both the present and future scenarios, there seem to be no problem of access to the test itself.

We use internet to denote both public (the Internet) and private interconnected networks.
APPENDIX: DISCUSSION QUESTIONS

1. What ethical risks might there be in the development of genomic testing?
2. Who should be allowed to see and use genetic genomic test results for what purpose and under what conditions?
3. What if our cultural ethos did not uphold privacy and instead all information was public?
4. Who are the stakeholders of genomic information?
5. Is there another way to analyze the “results” of the application of the four principles described in the chapter?
6. The conclusion suggests that the “Argument from prudence” is sound: we should move slowly. But even if we do, how are we to recognize moral pitfalls before jumping into them?
7. What special role do IAS professionals have in terms of the ethical treatment of genetic information?
8. Why are these four principles important?
9. What are the similarities and differences between the four principles presented in this chapter and the classical ethical theories presented in chapter two and what might that mean for considering ethical risks of pharmacogenomic testing for drug efficacy?
10. What is the requirement of system designers with regard to genomic information systems?
11. To implement the policy surrounding genetic testing, which approach is better? Top-down or bottom-up? What is your justification?
12. Should we uphold the individual’s right to privacy over the public good of the portability of medical data?
13. What is the ethical relationship between genetic testing for disease prediction and pharmacogenomic testing?
14. Is it preferable to store just a person’s SNPs or the person’s more detailed genetic information for the purpose of pharmacogenomic testing for drug efficacy?
15. Is there another way to analyze the “results” of the application of these four principles?
16. Consider and compare the following two cases:
   a. A mother is diagnosed with a genetic predisposition for Parkinson’s disease. Her daughter is deciding whether to get the test. What are the ethical risks associated with her diagnosis?
   b. A mother is diagnosed as needing a higher dose of heart medication. Her daughter is at risk of a similar heart condition as her mother. What are the ethical risks associated with pharmacogenomic testing to calculate appropriate drug dosage for her?
17. What are the advantages and disadvantages of pharmaceutical corporations as stakeholders in pharmacogenomic testing? Consider both that pharmaceutical companies may not produce drugs for “orphan genotypes” but also may reproduce orphaned drugs! How might this absolve access issues?