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The Brave New World of Genetic Biobanks: International Lessons for a Potential United States Biobank

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THE BRAVE NEW WORLD OF GENETIC BIOBANKS: INTERNATIONAL LESSONS FOR A POTENTIAL UNITED STATES BIOBANK

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Alpha children wear gray. They work much harder than we do, because they're so frightfully clever. I'm really awfully glad I'm a Beta, because I don't work so hard. And then we are much better than the Gammas and Deltas. Gammas are stupid. They all wear green, and Delta children wear khaki. Oh no, I don't want to play with Delta children. And Epsilons are still worse. . . . They're too stupid to be able to read or write. Besides they wear black, which is a beastly colour. I'm so glad I'm a Beta.[1]

I. INTRODUCTION

The search for genetic links to human diseases has been a fascinating medical drama in the past two decades. Genetic science offers incredible potential to unlock the mysteries of an individual's current and future health risks and to produce medical tools that can predict, treat, and even cure disease. However, as researchers discover more about genetic links to disease, the relationship between genetic information and diseases appears to grow more complicated.[2] It is now known that deoxyribonucleic acid ("DNA") causes not only single-gene disorders such as Huntington's Disease, but also multifactorial and polygenic diseases,[3] in which a physical response is produced by a combination of multiple genes and environmental factors, and even predispositions or

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[1] ALDOUS HUXLEY, BRAVE NEW WORLD 27–28 (Harper Perennial Modern Classics ed., HarperCollins Publishers 2006) (1932) (quoting "the trumpet" speaker system in Aldous Huxley's *Brave New World*). Huxley's novel details a futuristic world that has manipulated reproductive technology to create a utopian society separated into a caste system. *Id. Brave New World* warns of technology loosed without moral limits in place to protect us from ourselves. *Id*.

[2] Henry T. Greely, *Iceland's Plan for Genomics Research: Facts and Implications*, 40 JURIMETRICS J. 153, 155 (2000) [hereinafter Greely, *Iceland's Plan*].

[3] *See Genetic Disease Information* – pronto!, HUM. GENOME PROJECT INFO., http://www.ornl.gov/sci/techresources/Human_Genome/medicine/assist.shtml (last modified July 21, 2008) (providing a quick overview of genetic disorders).

susceptibilities to disease.[4] Small, family-based studies can be useful for linking genetic variations to disease that "always have a genetic cause and where one genotype is completely penetrant"; however, they prove of little use in the majority of cases because multiple genes and environmental factors are implicated.[5] Identification of genetic variants related to complex diseases requires correlation of genetic and non-genetic data in larger human populations. A better strategy to link genetic variations to complex diseases is to gather genetic, medical, and environmental data on a multitude of individuals and use the data to find relationships between all factors.

One way to achieve this strategy would be to implement a nationwide genetic biobank. A genetic biobank is "a stored collection of genetic samples in the form of blood or tissue, that can be linked with medical and genealogical or lifestyle information from a specific population, gathered using a process of generalized consent."[6] Alternately, such databases are "collections of genetic sequence information, or of human tissue from which such information might be derived that are or could be linked to named individuals."[7] Biobanks facilitate large-scale research. Some scientists consider a nationwide genetic biobank to be the "logical next step that would build on the complete sequencing of the human genome to enhance the understanding of common diseases and improve treatments and therapies" for disease.[8] Long-term, large cohort studies made possible by a nationwide genetic biobank "may permit researchers to decipher the interplay between genes, the disease and the environment."[9] For this reason, the National Institutes of Health ("NIH") in the United States has begun an investigation into the initial questions concerning the possibility of mounting a new large U.S. cohort study that would necessarily involve the construction of a genetic biobank for the United

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4 Angela Brand, Helmut Brand & Tobias Schulte in den Bäumen, *The Impact of Genetics and Genomics on Public Health*, 16 EUR. J. HUM. GENETICS 5, 8 (2008).

5 Greely, *Iceland's Plan*, *supra* note 2, at 156.

6 Melissa A. Austin, Sarah Harding & Courtney McElroy, *Genebanks: A Comparison of Eight Proposed International Genetic Databases*, 6 COMMUNITY GENETICS 37, 37 (2003).

7 J.V. McHale, *Regulating Genetic Databases: Some Legal and Ethical Issues*, 12 MED. L. REV. 70, 71 (2004) (citing SCI. & TECH. COMM., HOUSE OF LORDS, FOURTH REPORT ¶ 3.3 (Mar. 2001) (U.K.)), *available at* http://www.parliament.the-stationery-office.co.uk/pa/ld200001/ldselect/ldsctech/57/5701.htm).

8 SEC'YS ADVISORY COMM. ON GENETICS, HEALTH & SOC'Y, DEP'T OF HEALTH & HUMAN SERVS., POLICY ISSUES ASSOCIATED WITH UNDERTAKING A NEW LARGE U.S. POPULATION COHORT STUDY OF GENES, ENVIRONMENT, AND DISEASE 1 (2007) [hereinafter POLICY ISSUES], (footnote omitted), *available at* http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_LPS_report.pdf.

9 McHale, *supra* note 7, at 71.

States.[10] In addition, in 2006, then-Senator Barack Obama called for the establishment of a national biobanking initiative when he introduced the Genomics and Personalized Medicine Act.[11] That proposed legislation would have required the Secretary of the Department of Health and Human Services ("DHHS") to "establish a system for the integration of data, including genomic data and associated environmental and clinical health information" for the U.S. population.[12]

A U.S. genetic biobank would have to find public support to be successful, so it must overcome fears of misuse and abuse. One common concern is that third parties will use genetic information to the detriment of individual participants of the biobank—for example, to discriminate in employment or insurance on the basis of genetic information; to deny the individual access to health insurance completely; or, in the extreme, to manipulate genes in order to create a genetically stratified world like the one described in the movie *Gattaca* or in the quote from Aldous Huxley's *Brave New World* that began this Article.[13] The public health agencies that would control a genetic biobank must convince the population that a biobank does not seek to modify genes and that protections are in place to safeguard individuals.[14]

To lay a foundation of trust with the public—a necessary participant in a genetic biobank—the United States can start by addressing four key ethical issues presented by biobanks: (1) confidentiality and privacy of

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10 POLICY ISSUES, *supra* note 8, at 17–21. To achieve maximum scientific results, a large biobank unique to the United States would be necessary. Researchers should not generalize the findings from one small community to the entire United States given the enormous cultural and environmental diversity present. Ellen Wright Clayton, *The Complex Relationship of Genetics, Groups, and Health: What It Means for Public Health*, 30 J.L. MED. & ETHICS 290, 294 (2002). Similarly, findings from Iceland or Estonia cannot be generalized to the much more diverse population living in the United States existing in different environmental conditions. *Id*. "[A]lthough a potential new effort could seek to build on existing cohorts, new data collection and expanded consent would be needed from all study participants, and a new study design and infrastructure would be necessary." NAT'L HUM. GENOME RES. INST., NAT'L INSTS. OF HEALTH, DESIGN CONSIDERATIONS FOR A POTENTIAL UNITED STATES POPULATION-BASED COHORT TO DETERMINE THE RELATIONSHIPS AMONG GENES, ENVIRONMENT, AND HEALTH: RECOMMENDATIONS OF AN EXPERT PANEL 4 (2005) (parenthetical omitted), *available at* http://www.genome.gov/Pages/About/OD/ReportsPublications/PotentialUSCohort.pdf. Therefore, the new cohort would face all the issues presented in this Article.

11 Genomics and Personalized Medicine Act of 2006, S. 3822, 109th Cong. (2006).

12 *Id.* § 5(a)(2)(B)(i).

13 Ellen Wright Clayton, *Ethical, Legal, and Social Implications of Genomic Medicine*, 349 NEW ENG. J. MED. 562, 562 (2003). *See generally* HUXLEY, *supra* note 1; GATTACA (Columbia Pictures 1997) (describing a futuristic world that has manipulated reproductive technology).

14 Angela Brand, *Public Health and Genetics – A Dangerous Combination?*, 15 EUR. J. PUB. HEALTH 114, 115 (2005).

information; (2) informed consent by the individual; (3) feedback of clinically significant information; and (4) the treatment of humans as research subjects. This Article will address these four issues by looking at how three international leaders in genetic biobanking—Iceland, Estonia, and the United Kingdom—dealt with these ethical problems.[15] Part II will introduce the three nations' international biobanks. Part III will explore the four ethical issues and discuss how each international biobank addressed the issue and how their responses may translate to a U.S. biobank. Because the treatment of humans as research subjects hinges on informed consent,[16] those issues will be examined together. Finally, Part IV will propose that a nationwide biobank be instituted in the United States.

II. INTERNATIONAL BIOBANKS

Three European nations are at the forefront of the genetic biobank movement: Iceland, Estonia, and the United Kingdom. The following sections will provide a short background of these international banks and their operations.

A. Iceland

Due to its relative isolation and small, homogenous population of only 270,000, which results in less genetic variation, Iceland has been described as an "island so inbred that it is a happy genetic hunting ground."[17] In addition, Iceland keeps extensive medical records on its population going back to 1915 that would aid researchers in their quest to link genetic variations to disease in an individual.[18] Furthermore, because genealogy is so important to Icelandic culture, an extensive genealogical database exists that stretches as far back as 900 A.D., allowing scientists to "find a common ancestor between two people with

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15 *See* Susan M.C. Gibbons et al., *Lessons from European Population Genetic Databases: Comparing the Law in Estonia, Iceland, Sweden and the United Kingdom*, 12 EUR. J. HEALTH L. 103, 104 (2005).

16 *See* Henry T. Greely, *The Uneasy Ethical and Legal Underpinnings of Large-Scale Genomic Biobanks*, 8 ANN. REV. GENOMICS & HUM. GENETICS 343, 353 (2007) [hereinafter Greely, *Genomic Biobanks*].

17 MATT RIDLEY, GENOME: THE AUTOBIOGRAPHY OF A SPECIES IN 23 CHAPTERS 190–91 (1999).

18 POLICY ISSUES, *supra* note 8, at D-4.

the same disease" or condition.[19] For these reasons, the island nation contains a near perfect population for genetic research.[20]

Iceland acted on these advantages in December 1998 by creating the first national genetic biobank when the Icelandic parliament, the Althingi, passed the Act on a Health Sector Database ("HSD Act").[21] The objective of the HSD Act was to "authorise the creation and operation of a centralised database of non-personally identifiable health data with the aim of increasing knowledge in order to improve health and health services."[22] At its core, the HSD Act authorizes the creation of a Health Sector Database ("HSD"), which is "[a] collection of data containing information on health and other related information, recorded in a standardised systematic fashion on a single centralised database, intended for processing and as a source of information."[23]

The HSD Act, however, did not actually create a biobank; in fact, it expressly disclaimed such a creation by stating that "[t]he legislation does not apply to the storage or handling of, or access to, biological samples."[24] The HSD is merely a collection of medical records of the Icelandic people. The actual creation of the genetic biobank, and of the HSD, would be done by a licensee operating under the terms of the HSD Act.[25] In 2000, the Althingi granted a twelve-year license to construct and manage an electronic database for all of Iceland's health records to deCode genetics, Inc. ("deCode"), a private commercial company with American and Icelandic ties, that apparently instigated the creation of the HSD Act.[26] In short, deCode was granted a license to create an electronic database that would contain extensive medical information on each Icelander and to connect that database with Iceland's genealogy database.[27] Iceland also granted deCode a third database that would be created privately by deCode that would consist of genetic samples from volunteers within the Icelandic population.[28] An individual could opt out of the genetic database by express statement to deCode,[29] a provision

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19 *Id.* at A-6.

20 *See* Greely, *Iceland's Plan*, *supra* note 2, at 157–61 (providing an extensive history that details why Iceland contains a geneticist's dream population).

21 Act on a Health Sector Database, No. 139/1998 (1998) (Ice.), *available at* http://eng.velferdarraduneyti.is/acts-of-Parliament/nr/17659#kafli1.

22 *Id.* § I, art. 1.

23 *Id.* § I, art. 3, cl. 1.

24 *Id.* § I, art. 2.

25 *Id.* § II, art. 4.

26 Yael Bregman-Eschet, Note, *Genetic Databases and Biobanks: Who Controls Our Genetic Privacy?*, 23 SANTA CLARA COMPUTER & HIGH TECH. L.J. 1, 38 (2006).

27 *Id*.

28 *Id.*

29 *Id.* at 41.

that only 20,000 of Iceland's 270,000 citizens took advantage of within the first four years of the license.[30] To date, though, no comprehensive database has yet materialized, but important lessons can be learned from Iceland's cardinal attempt.

B. Estonia

Estonia's parliament, Riigikogu, passed the Human Genes Research Act in December 2000, launching the Estonian Genome Project ("EGP").[31] The EGP is a national genetic biobank that also contains medical information such as lifestyle reports, demographics, and genealogy.[32] The EGP Foundation, a nonprofit foundation created by the Republic of Estonia in 2001, legally owns the biobank.[33] The Foundation is the true owner of the database and acts as a privacy shield, but a for-profit company created by the foundation, EGeen, is the exclusive licensee of the biobank and has the rights to set up and sell access to the information collected.[34] The EGP Foundation "has the right to organise [sic] the taking of DNA samples, to prepare descriptions of health status and genealogies, to code and decode, preserve, destroy and issue descriptions of health status and genealogies, to perform genetic research and to collect, preserve, destroy and issue genetic data"; all of these rights, except for the right to code and decode information, have been delegated to EGeen.[35] The biobank is expected to include nearly one million of Estonia's 1.4 million people.[36] A small test run of 10,000 people has been conducted under a pilot program,[37] and to date, over 40,000 participants have donated samples to the biobank.[38]

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30 Geneviève Cardinal & Mylène Deschênes, *Surveying the Population Biobankers*, *in* POPULATIONS AND GENETICS: LEGAL AND SOCIO-ETHICAL PERSPECTIVES 37, 40 (Bartha Maria Knoppers ed., 2003).

31 Andres Rannamäe, *Estonian Genome Project – Large Scale Health Status Description and DNA Collection*, *in* POPULATIONS AND GENETICS, *supra* note 30, at 17, 18; *see also* Human Genes Research Act (RT I 2000, 104, 685) (2001) (Est.) (creating the EGP).

32 POLICY ISSUES, *supra* note 8, at D-4. *See generally* ESTONIAN GENOME CTR., http://www.geenivaramu.ee/index.php? lang=eng (last visited Apr. 7, 2011) (providing an English-language website operated by the EGP).

33 Cardinal & Deschênes, *supra* note 30, at 39.

34 Rannamäe, *supra* note 31, at 18.

35 *Id.* at 24.

36 Riku Lähteenmaki, *Estonian Parliament Considers Genome Law*, 18 NATURE BIOTECHNOLOGY 1135, 1135 (2000).

37 Greely, *Genomic Biobanks*, *supra* note 16, at 348.

38 *What is the Genome Center?*, ESTONIAN GENOME CTR., http://www.geenivaramu.ee/index.php?id=102 (last visited Apr. 7, 2011).

C. United Kingdom

Unlike the biobanks in Iceland and Estonia, the project in the United Kingdom does not exist due to a single national piece of legislation, and it does not plan to include a vast majority of the population.[39] The UK project, termed UK Biobank, plans to enroll as many as half a million volunteers age forty-five to sixty-nine.[40] The project was finally launched in March 2006 after six years of planning.[41] A pilot run of nearly four thousand residents from Manchester was declared a success in the summer of 2006, so UK Biobank is now collecting information and samples from volunteers.[42] The Biobank is a collaboration between the UK Medical Research Council, the Department of Health, and the Wellcome Trust, which is the United Kingdom's largest independent medical research charity.[43] Tom Meade, director of the Medical Research Council Epidemiology and Medical Care Unit, stresses that, unlike the Iceland biobank that is run by a commercial company, UK Biobank is controlled by "independent research organizations."[44] No legislation or guidelines relate specifically to UK Biobank.[45]

Through research, UK Biobank strives to understand how genetic, lifestyle, and environmental risk factors contribute to disease, both as discrete factors and through their combined effects.[46] It is designed to be a longitudinal prospective cohort study that will follow the volunteers for ten years.[47] UK Biobank is particularly concerned with "diseases of later life, such as cancer and cardiovascular conditions," leading to the narrow age range of the project.[48] As in Iceland, the project will be immensely aided by medical records kept by the UK National Health Service, which "treats the single largest group of people anywhere in the world."[49] The UK Biobank-driven study "is to be in 'public ownership'

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39 *See Improving the Health of Future Generations,* BIOBANK[UK], http://www.ukbiobank.ac.uk/ (last visited Apr. 7, 2011) (explaining that the genesis of this biobank lies with independent research charities as well as the government).

40 Mylène Deschênes & Clémentine Sallée, *Accountability in Population Biobanking: Comparative Approaches*, 33 J.L. MED. & ETHICS 40, 41 (2005).

41 *See* Kathryn Senior, *UK Biobank Launched to Mixed Reception*, 5 LANCET NEUROLOGY 390, 390 (2006).

42 Greely, *Genomic Biobanks*, *supra* note 16, at 348.

43 Frances C. Rawle, *UK DNA Sample Collections for Research*, *in* POPULATIONS AND GENETICS, *supra* note 30, at 3.

44 Michael Hagmann, *U.K. Plans Major Medical DNA Database*, 287 SCI. 1184, 1184 (2000).

45 *See* Cardinal & Deschênes, *supra* note 30, at 41.

46 Rawle, *supra* note 43, at 3.

47 Cardinal & Deschênes, *supra* note 30, at 41.

48 McHale, *supra* note 7, at 72.

49 Claire Tilstone, *Further Plans Announced for National Biobanks*, 7 LANCET ONCOLOGY 195, 195 (2006) (quoting Rory Collins, principal investigator for UK Biobank).

through the operation of a new independent body created by [the Medical Research Council, the Wellcome Trust], and the [Department of Health] called 'Hubco.'"[50] Outside researchers can obtain anonymized data from Hubco if approved by a research ethics committee.[51]

III. FOUR MAJOR ETHICAL ISSUES IN POPULATION BIOBANKS

Genetic biobanks present unique ethical issues that traditional biomedical research does not present. Traditional research involves a single researcher or an established group of researchers who obtain and utilize samples in defined ways after obtaining informed consent from each individual research subject for that use.[52] For example, one laboratory at a university may ask cancer patients to test a new treatment. The scientists would ask for a single blood sample to determine serum titer to test how the treatment is affecting immune cells. The researchers would be dealing with a defined small group of consenting individuals for an identified disease. In contrast,

> with biobanks: (1) the individual or entity obtaining the sample may not be engaged in research, but may be only a broker or intermediary supplying specimens to other researchers; (2) the purpose of a biobank is to develop a repository that can be used for many research protocols, often in numerous scientific areas; (3) a biobank contemplates future research activities, including research by investigators who cannot be specified at the time of the sample collection; and (4) research using biobanks seeks to move beyond the one study/one informed consent model.[53]

A national biobank must deal with these issues to be successful and to comply with ethical and legal standards. Bioethicist Henry T. Greely has placed these unique concerns into groupings that will guide the discussion in the following sections: (1) confidentiality and privacy; (2) informed consent and humans as research subjects; and (3) feedback of clinically significant information.[54]

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50 McHale, *supra* note 7, at 72.

51 *Id.*

52 Mark A. Rothstein, *Expanding the Ethical Analysis of Biobanks*, 33 J.L. MED. & ETHICS 89, 89 (2005).

53 *Id.*

54 *See* Greely, *Genomic Biobanks*, *supra* note 16, at 349.

A. Confidentiality and Privacy

The World Medical Association states, "[t]he right to privacy entitles people to exercise control over the use and disclosure of information about them as individuals."[55] Though privacy and confidentiality are often used interchangeably, their meanings differ slightly. Privacy covers, *inter alia*, access to one's biological sample or general medical information.[56] Confidentiality, in contrast, generally connotes nondisclosure of private, identifiable information to third parties.[57] Because informed consent and access to the biological sample will be discussed in the next section, this section will focus on the nondisclosure of private information after access to that information has been granted through informed consent.

Genes present a variety of unique problems to researchers in terms of confidentiality. While genes can identify an individual's place in the gene pool, they can also reveal the place of others.[58] Family members share genetic information. For example, a genetic sample from one individual would reveal many genes shared by that person's mother, father, brothers, sisters, and so on. This expected familial linkage, though, could also lead to realization that some family members are not, in fact, family at all. As Greely puts it, "[c]omparing genomic information from two people thought to be related could lead to some unpleasant surprises, breaking families or blighting careers."[59] Genetic information also provides information unique to the individual, including much of the information sought by researchers—for example, propensities for future disease. This information may cause worries about discrimination as a result of disclosure or loss of medical insurance. Furthermore, exposure of an individual's medical information carries the usual worries of disclosure of health data—revelations of substance abuse or sexually transmitted infections, for instance.

Complete anonymization could protect the genetic and medical information, but this approach would greatly decrease the viability of a

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55 World Med. Ass'n, *WMA Declaration on Ethical Considerations Regarding Health Databases* 1, ¶ 1 (2002), *available at* http://www.wma.net/en/30publications/10policies/d1/index.html.pdf?print-media-type&footer-right=[page]/[toPage].

56 *See* Mary R. Anderlik & Mark A. Rothstein, *Privacy and Confidentiality of Genetic Information: What Rules for the New Science?*, 2 ANN. REV. GENOMICS & HUM. GENETICS 401, 402 (2001) (discussing the broad concept of privacy).

57 John A. Robertson, *Ethical and Legal Issues in Genetic Biobanking*, *in* POPULATIONS AND GENETICS, *supra* note 30, at 297, 302.

58 Sheila A.M. McLean, *The Genetics Revolution: Can the Law Cope?*, *in* GENETICS & ETHICS 35, 43 (Gerard Magill ed., 2004).

59 Greely, *Genomic Biobanks*, *supra* note 16, at 350.

biobank. Anonymization strips "the information of all identifiers, trying to make it impossible for anyone . . . to establish individual identities."[60] Unfortunately, this method also makes it impossible for a biobank researcher or manager to identify the individual, severely limiting the usefulness of the samples or data in research.[61] According to the NIH, "in a longitudinal cohort study, anonymity is not possible because it would prevent the collection of additional health status and exposure information in later phases."[62] Researchers must be able to connect genetic information to the individual. In addition, anonymization may not even prove that safe. This was proven by a recent appointee to the privacy and security seat of the Health Information Technology Policy Committee, Professor Latanya Sweeney, while she was completing her doctorate at the Massachusetts Institute of Technology. The State of Massachusetts made "anonymized medical information" available to the public, claiming it was safe because all means of identification had first been removed.[63] The medical data only contained the person's diagnosis, gender, birth date, and zip code.[64] Sweeney purchased a voter list from Cambridge City Hall for twenty-five dollars, linked the minimal demographic data with the information in the voter list, and successfully linked a single file to then-Governor William Weld within a few days.[65] This leak could have been avoided by removing even the minimal demographic data, but, again, that would lessen its scientific impact. In sum, "[t]he more data is removed . . .the more scientific value is lost; the more data is kept, the less the data is truly anonymized."[66]

The alternative to complete anonymization is key coding. This is the most widely used method of protecting confidentiality in health research because it allows the researcher to update the data set.[67] When data are key coded, the identifying information is separated from the substantive data—in this case, the genetic and medical information—but the biobank maintains a link between the two data sets by marking each set with a random, arbitrary code number.[68] This code would be kept in a secure

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60 *Id.* at 351.

61 *See* Rothstein, *supra* note 52, at 94.

62 POLICY ISSUES, *supra* note 8, at 57.

63 Greely, *Genomic Biobanks*, *supra* note 16, at 352.

64 Jonathan Shaw, *Exposed: The Erosion of Privacy in the Internet Era*, HARV. MAG., Sept.–Oct. 2009, at 39.

65 *Id.*

66 Greely, *Genomic Biobanks*, *supra* note 16, at 353.

67 WILLIAM W. LOWRANCE, NAT'L HUMAN GENOME RESEARCH INST., PRIVACY, CONFIDENTIALITY, AND IDENTIFIABILITY IN GENOMIC RESEARCH 17 (Oct. 3, 2006), *available at* http://www.genome.gov/Pages/About/OD/ReportsPublications/IdentifiabilityWorkshopWhitePaper.pdf.

68 *Id.*

location and would not normally be accessible to the researcher.[69] The researcher would have to go through a trusted intermediary to obtain updates on the file.[70] Like other confidential data sets, the key coding system could be misused by rogue biobank officials or stolen by third parties. Criminal sanctions could be threatened, however, to mitigate these threats. Each nation studied in this Article uses some type of key coding system.

The Data Protection Commission ("the Commission") runs the key coding system for Iceland's biobank.[71] According to the HSD Act,

> Personal identification shall be coded before entry on the database, so that it is ensured that the licensee's staff work[s] only with non-personally identifiable data. . . . Health data shall be transferred in coded form in order to ensure their security. Personal identification shall be coded one-way, i.e. by coding that cannot be traced using a decoding key. The Data Protection . . . [Commission] shall carry out further coding of personal identification, using those methods that the commission deems to ensure confidentiality best.[72]

In essence, personnel at the licensed health institution gather the health information, code it, and transfer it in non-personally identifiable form to the database operator.[73] Then, the database operator who compiles information for the biobank enters the coded data into the bank. He is not able to link the data to any specific individual; only the Commission holds the encrypted identification number.[74] To link this data with its genetic and genealogical databases, deCode would need the encrypted identification numbers from the Commission. The HSD Act provides for access to the key with some major limitations:

> The licensee [deCode] shall be authorised to process data on the health sector database from the health data recorded there, provided that data are processed and

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69 Greely, *Genomic Biobanks*, *supra* note 16, at 350.

70 *See id.* at 351 (describing the procedures of coding whereby researchers only receive a code to identify a sample that they cannot directly trace to a particular individual).

71 Act on a Health Sector Database, No. 139/1998, § III, art. 7 (1998) (Ice.), *available at* http://eng.velferdarraduneyti.is/acts-of-Parliament/nr/17659#kafli1.

72 *Id.*

73 Alice Hsieh, Note, *A Nation's Genes for a Cure to Cancer: Evolving Ethical, Social and Legal Issues Regarding Population Genetic Databases*, 37 COLUM. J.L. & SOC. PROBS. 359, 385–86 (2004).

74 *Id.*

> connected in such a way that they cannot be linked to identifiable individuals. The licensee shall develop methods and protocols that meet the requirements of the [Commission] in order to ensure confidentiality in connecting data from the health-sector database, from a database of genealogical data, and from a database of genetic data. . . . The licensee may not grant direct access to data on the database.[75]

As part of its exclusive license, deCode must develop procedural rules for cross-referencing of data between databases, and those rules must be approved by the Commission.[76] All storage and processing of data must take place in Iceland, and only the approved licensee may have direct access to the data.[77] As a result of these restrictions, however, *someone* at deCode will eventually have to make the link between the coded health data and the genealogical data, opening the door for a possible breach of confidentiality.[78] Because employment of Icelanders was a major selling point for deCode in bidding for the exclusive license, chances are that an Icelander will be in control of this knowledge.[79] Iceland is a relatively small nation, so the employee stands a greater chance of knowing the research subject.[80] The HSD Act attempts to control potential leaks by requiring an oath of confidentiality from each of the licensee's employees that continues even after employment ceases.[81] Furthermore, the HSD Act provides for compensation to victims of a security breach to be paid by the licensee.[82] In other words, deCode would be held liable for actions taken by malevolent employees.

Estonia also uses a coding system, but with an added layer of security for personal information. An authorized data collector gathers phenotypic or health data first; this includes information on health status, genealogy, lifestyle, environmental factors, and drug response.[83] Next, the data collector takes a tissue sample from the donor for the DNA collection. These data are given a unique temporary transportation

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75 Act on a Health Sector Database § IV, art. 10 (Ice.).
76 Cardinal & Deschênes, *supra* note 30, at 67.
77 § IV, art. 10.
78 Greely, *Iceland's Plan*, *supra* note 2, at 184.
79 *Id.* at 185–86.
80 *Id.* at 186.
81 Act on a Health Sector Database § IV, art. 11 (Ice.).
82 *Id.* § VI, art. 17.
83 Rannamäe, *supra* note 31, at 26.

code.[84] This code is replaced at the storage facility by the database processor who assigns a permanent sixteen-digit code so that the collection agent cannot connect the genetic information with the personal identity of the donor.[85] For an additional level of security, the phenotypic data is stripped of personal identifiers, such as names, birth dates, and addresses, and given a second code saved in a separate database of personal data.[86] This double coding system allows researchers to link genetic data with health data without being able to see personal data that could easily identify the research subject. That data can only be connected back to the person under limited circumstances—to find the donor to correct erroneous genealogical data, for instance.[87] Researchers will only handle coded, identity-free data; only persons appointed by the EGP handle the coding and decoding duties.[88]

Despite assurances from UK Biobank that DNA samples and information are stored anonymously,[89] the UK project actually uses a basic coding system, misleadingly termed "reversible anonymisation."[90] "[P]ersonal identifying information [is] separated from participants' data and samples and . . . linked [with] a code that has no external meaning."[91] This is the quintessential coding system. Only a few UK Biobank staff operating under strict confidentiality pledges hold the code key for re-linking information, and researchers will not be given access to the key.[92]

Over one hundred bills specifically targeting genetic privacy have been introduced in Congress, but none have been signed into law; the United States thus has no federal laws on the issue.[93] Nevertheless, a legal framework for the protection of private information does exist. First, federal agencies have guidance on using a coding system in human

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84 *Id.* at 30.

85 Hsieh, *supra* note 73, at 386; *see also Main Provisions of the Human Genes Researsh* [sic] *Act*, ESTONIAN GENOME CTR., http://www.geenivaramu.ee/index.php?id=105 (last visited Apr. 7, 2011) [hereinafter *Main Provisions*] (detailing guidelines pertaining to the establishment and maintenance of the Gene Bank).

86 Rannamäe, *supra* note 31, at 30.

87 *Id.* at 33.

88 Cardinal & Deschênes, *supra* note 30, at 66.

89 *See Confidentiality*, BIOBANK[UK], http://www.ukbiobank.ac.uk/faqs/confidentiality.php (last visited Apr. 7, 2011) (answering frequently asked questions about privacy and third-party access to the information).

90 UK BIOBANK, UK BIOBANK ETHICS AND GOVERNANCE FRAMEWORK VERSION 3.0 11 (Oct. 2007), *available at* http://www.ukbiobank.ac.uk/docs/EGF20082.pdf.

91 *Id.*

92 *Id.*

93 DOROTHY C. WERTZ & JOHN C. FLETCHER, GENETICS AND ETHICS IN GLOBAL PERSPECTIVE 170 (2004).

research. The U.S. Office of Human Research Protections ("OHRP") defines "coded" as:

> (1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and
> (2) a key to decipher the code exists, enabling linkage of the indentifying information to the private information or specimens.[94]

If a national biobank were created, this guidance could be used as a foundation for rules on codifying personal information of participants.

Second, a right to privacy has been generally recognized by the Supreme Court as a fundamental right under the Fourteenth Amendment Due Process Clause, though privacy is not explicitly mentioned in the Constitution.[95] In *Griswold v. Connecticut*, the Supreme Court of the United States initially found that "specific guarantees in the Bill of Rights have penumbras, formed by emanations from those guarantees that help give them life and substance. Various guarantees create zones of privacy."[96] The Court has since declared that the right of privacy is founded in the Fourteenth Amendment's concept of personal liberty.[97]

In *Whalen v. Roe*, the Court addressed what privacy means for medical information when it stated the following: "The cases sometimes

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[94] OFFICE FOR HUMAN RESEARCH PROTS., U.S. DEP'T OF HEALTH & HUMAN SERVS., GUIDANCE ON RESEARCH INVOLVING CODED PRIVATE INFORMATION OR BIOLOGICAL SPECIMENS 3 (2008) [hereinafter OHRP], *available at* http://www.hhs.gov/ohrp/policy/cdebiol.pdf.

[95] U.S. CONST. amend. XIV, § 1. In language reminiscent of the Fifth Amendment's guarantee of liberty against intrusion by the federal government, the Fourteenth Amendment states, in part, "nor shall any State deprive any person of life, liberty, or property, without due process of law." *Id*.

[96] 381 U.S. 479, 484 (1965) (citation omitted).

[97] *See* Roe v. Wade, 410 U.S. 113, 152–53 (1973) ("[T]he Court has recognized that a right of personal privacy, or a guarantee of certain areas or zones of privacy, does exist under the Constitution. . . . [including] in the concept of liberty guaranteed by the first section of the Fourteenth Amendment." (citations omitted)). Though *Roe* involved a challenge to state law under the Fourteenth Amendment's prohibition on state actions, it has been assumed to apply to the federal government through the Due Process Clause of the Fifth Amendment as well. *See* Lawrence v. Texas, 539 U.S. 558, 578–79 (2003) (applying the right of privacy to states through the Due Process Clause of the Fifth and Fourteenth Amendments).

characterized as protecting 'privacy' have in fact involved at least two different kinds of interests. One is the individual interest in avoiding disclosure of personal matters, and another is the interest in independence in making certain kinds of important decisions."[98] The first type of privacy listed by the Court concerns confidentiality; the second type deals with informed consent, which will be discussed in the following section. Despite the seemingly unfettered privacy right hinted at in *Griswold*, the Court in *Whalen* limited the protections afforded by the Due Process Clause over the interest in keeping medical information private. As Justice Powell pointed out,

> *Griswold v. Connecticut* held that a State cannot constitutionally prohibit a married couple from using contraceptives in the privacy of their home. Although the broad language of the opinion includes a discussion of privacy, the constitutional protection there discovered also related to (1) marriage; (2) privacy *in the home*; and (3) the right to use contraceptives. Whatever the *ratio decidendi* of *Griswold*, it does not recognize a general interest in freedom from disclosure of private information.[99]

In other words, while *Griswold* offers constitutional protection that may be extended to personal medical information, that right is not absolute. The Constitution does not categorically prohibit government intrusion on the right of privacy implicated here. The majority opinion in *Whalen* points out that disclosure of private medical information to third parties, such as doctors and public health agencies, is an essential reality of the modern health system, "even when the disclosure may reflect unfavorably on the character of the patient."[100] The threat of wrongful, unwarranted disclosure of that information is not enough to block government collection of the information as long as proper security measures and judicial supervision is in place.[101] Indeed, many government actions require the collection of such information, including the "collection of taxes, the distribution of welfare and social security benefits, the supervision of public health, the direction of our Armed Forces, and the enforcement of the criminal laws."[102]

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98 429 U.S. 589, 599–600 (1977) (footnotes omitted).
99 *Id.* at 608–09 (Stewart, J., concurring) (internal citations omitted).
100 *Id.* at 602 (majority opinion).
101 *Id.* at 600–01.
102 *Id.* at 605.

The Court's analysis seems to assume a constitutional interest in privacy of medical information; however, it never explicitly states that this is true or how important such an interest might be. Rather, the Court appears to assume the right for purposes of the decision. The Third Circuit offers a little more guidance on the issue in *United States v. Westinghouse Electric Corp.*, stating that government "intrusion into the zone of privacy surrounding medical records" can be entered if the societal interest in disclosure outweighs the privacy interest in a specific case.[103] Seven factors must be weighed in determining whether an intrusion into an individual's privacy is justified:

> the type of record requested, the information it does or might contain, the potential for harm in any subsequent nonconsensual disclosure, the injury from disclosure to the relationship in which the record was generated, the adequacy of safeguards to prevent unauthorized disclosure, the degree of need for access, and whether there is an express statutory mandate, articulated public policy, or other recognizable public interest militating toward access.[104]

If a future court used these factors to consider the constitutionality of a genetic biobank, insofar as the government's incursion on private medical records is at issue, the biobank stands a fair chance of success as long as the government implements a secure coding system supplemented by statutory remedies for security violations. This should ensure the adequacy of safeguards as required in the test. The degree of need for access should not present a hurdle for biobanks. As discussed previously, the research viability of a genetic biobank greatly decreases without access to personal health data. A genetic biobank would require complete access to private medical information to be useful. Furthermore, an agency implementing a national biobank would certainly be acting under an express statutory mandate or articulated public policy as the test favors. Conversely, the injury from disclosure may be lower than expected in the unlikely event that codified information is accidentally released to the general public or stolen by a third party. The law already shields most Americans from insurance or employment discrimination that stems from health-related information.[105]

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103 638 F.2d 570, 578 (3d Cir. 1980).

104 *Id.*

105 Greely, *Genomic Biobanks*, *supra* note 16, at 350.

A genetic biobank must ensure that private medical information remains confidential and private. Although the United States has no comprehensive law pertaining to genetic information,[106] the Supreme Court may offer constitutional protection against unwarranted violations of privacy. In addition, federal health agencies have guidance in place from the OHRP on using a coding system for sensitive information.

B. Informed Consent and Humans as Research Subjects

Informed consent affects the second part of privacy elucidated in *Whalen*—"the interest in independence in making certain kinds of important decisions."[107] This principle has been a pillar of medical research since World War II and the Nuremberg trials. The Nuremberg Code's principles for human research state that voluntary consent is essential.[108] The Code states the following:

> [Voluntary consent] means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice . . . and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision.[109]

The informed consent process involves three elements: (1) the information must be disclosed to potential participants; (2) the researcher

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[106] The Genetic Information Nondiscrimination Act allays some concerns over illicit use of genetic information by protecting against misuse by insurance companies and employers. *See* Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, 122 Stat. 881 (codified in scattered sections of 26, 29, and 42 U.S.C.) (prohibiting the discriminatory use of genetic information in the context of employment and health insurance). No statute protects against misuse of genetic information in other contexts, however.

[107] *Whalen*, 429 U.S. at 599–600.

[108] NUERNBERG MILITARY TRIBUNALS, TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY TRIBUNALS UNDER CONTROL COUNCIL LAW NO. 10, VOL. II 181–82 (1949), *available at* http://www.loc.gov/rr/frd/Military_Law/pdf/NT_war-criminals_Vol-II.pdf; *Directives for Human Experimentation: Nuremburg Code*, OFF. OF HUM. SUBJECTS RES., http://ohsr.od.nih.gov/guidelines/nuremberg.html (last visited Apr. 7, 2011). "The Nuremberg Code is judicial law created [for] . . . a specific historical situation," so it does not have legal force of legislative enactment. Markus Schott, *Medical Research on Humans: Regulation in Switzerland, the European Union, and the United States*, 60 FOOD & DRUG L.J. 45, 47–49 (2005). Still, the intention of the Nuremberg Code is to elucidate ethical principles of human research, and these principles have been endorsed by subsequent statements, such as the Declaration of Helsinki. *Id.*

[109] NUERNBERG MILITARY TRIBUNALS, *supra* note 108, at 181.

must ascertain that the participant understands what has been disclosed; and (3) the participant must voluntarily agree to participate in the research.[110] This means that the potential participant cannot be coerced or pressured into participating. Informed consent is essentially the "clinical version" of autonomy, an ethical axiom that respects the decision-making authority of the individual.[111] Concomitant with consent is the right of the individual to withdraw from the study.[112] The individual should retain autonomy in the process and not feel trapped or stripped of liberty for taking part in the research.[113]

Consent covers two important areas. The first is the main action in which the participant donates the genetic sample and submits to any medical and personal data collection.[114] The second covers any subsequent use of that genetic sample or the health data.[115] The problem for genetic biobanks is that subsequent uses are likely unknown at the time of sample collection.[116] Future research questions may not yet be conceptualized, and future researchers may not yet be involved in the biobank project.[117] A nationwide genetic biobank could be created for one particular and distinct research study, thereby conforming to traditional norms of medical research and informed consent.[118] This would be grossly expensive and a wasteful use of the available information. In fact, it would defeat the primary purpose of a biobank—to facilitate future research on the genetic factors of multiple diseases.[119] The alternative would be to seek out permission from each participant for every single new research study. This also appears prohibitively

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110 POLICY ISSUES, *supra* note 8, at 37–38.

111 Mark A. Rothstein, *Are Traditional Public Health Strategies Consistent with Contemporary American Values?*, 77 TEMP. L. REV. 175, 188–89 (2004).

112 Cardinal & Deschênes, *supra* note 30, at 49.

113 *See, e.g.*, George J. Annas, *Rules for Research on Human Genetic Variation—Lessons from Iceland*, 342 NEW ENG. J. MED. 1830, 1831 (2000) (arguing many scholars believe that "community consent" should also be required for nationwide genetic biobanks, because any findings of the biobank could characterize all citizens as a group); *see also* Henry T. Greely, *Informed Consent and Other Ethical Issues in Human Population Genetics*, 35 ANN. REV. GENETICS 785, 794 (2001) [hereinafter Greely, *Informed Consent*] (describing arguments for and against group consent). The political process in a democratic nation, though, should provide an important check on governments attempting to implement a biobank, thereby serving as the community consultation required to obtain group consent. This issue, therefore, will not be discussed in this Article. A vigorous public debate should suffice.

114 Carlos María Romeo Casabona, *Genetics, Tissue- and Databases*, 11 EUR. J. HEALTH L. 71, 72 (2004).

115 *Id.* at 72.

116 Gibbons et al., *supra* note 15, at 105.

117 POLICY ISSUES, *supra* note 8, at 38.

118 Gibbons et al., *supra* note 15, at 105–07.

119 *Id.*

expensive and time-consuming.[120] The challenge, then, for a genetic biobank is to implement a consent process that is broad enough to incorporate future research and uses of samples, but specific enough to comply with regulations and ethical objectives of informed consent principles.[121]

Iceland's HSD substitutes "presumed consent" for "informed consent" in the HSD Act.[122] Iceland set the default rule as inclusion, perhaps the most controversial piece of the entire project, and provided an opt-out procedure for citizens rather than the usual opt-in process.[123] Article Eight of the HSD Act speaks of the rights of "patients," but it never mentions consent. Instead, it states that "[a] patient may request at any time that information on him/her not be entered onto the health-sector database. The patient's request may apply to all existing information on him/her or that which may be recorded in the future, or to some specific information."[124] To opt-out of the database, Icelanders can file a form with the Director General of Public Health, who must make such forms available at health care centers.[125] One study, however, did not find the forms at two of three centers visited, implying that distribution of the forms may be an issue.[126]

This presumed consent, though, only applies to the health information and personal data collected for the medical information database created by the HSD Act. As discussed in Part II, the HSD Act did not actually create the genetic biobank that stores biological samples; that responsibility was licensed to deCode.[127] While Icelandic law may require informed consent from the individual for collection of a biological sample (i.e., the genetic sample),[128] deCode has decided to

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120 *Id*.

121 POLICY ISSUES, *supra* note 8, at 38.

122 Greely, *Informed Consent*, *supra* note 113, at 789.

123 Anderlik & Rothstein, *supra* note 56, at 410.

124 Act on a Health Sector Database, No. 139/1998, § III, art. 8 (1998) (Ice.), *available at* http://eng.velferdarraduneyti.is/acts-of-Parliament/nr/17659#kafli1.

125 *Id.*

126 Jon F. Merz et al., *"Iceland Inc."?: On the Ethics of Commercial Population Genomics*, 58 SOC. SCI. & MED. 1201, 1203 (2004).

127 *See supra* Part II.A (describing the HSD Act).

128 Gibbons et al., *supra* note 15, at 110. The type of consent necessary for collection of biological samples depends on whether the sample was obtained for donation to a biobank in the first instance or whether it was collected as part of a clinical diagnosis. *Id*. Scholars argue that this only suggests a presumed consent requirement for inclusion in the deCode database. *See* Cardinal & Deschênes, *supra* note 30, at 47 (describing the legislative exception that allows deCode to obtain biological samples without individual consent); *see also* Hsieh, *supra* note 73, at 378 ("The most controversial alternative to informed consent is the presumed consent provision of Iceland's Health Sector Database.").

require informed consent on its own for the genetic biobank.[129] This sets up two separate consent regimes for the Iceland project. First, Icelanders must opt-out of having their medical and personal data linked with genetic and genealogical data. The HSD Act assumes consent for this piece of the project.[130] Second, Icelanders must affirmatively give consent for inclusion in the genetic database. The licensee, deCode, requires informed consent for all individuals.[131]

Icelandic law states that consent to join a biological database can only be given for "clearly defined purposes," so it would appear that researchers would have to obtain further consent for future uses of the sample.[132] This may not be true, however, since the law also contains an exception granting the biobank broad discretion in authorizing subsequent uses of a biological sample under three conditions.[133] Those conditions include when: (1) significant interests are at issue; (2) the possible benefit eclipses the inconvenience to the donor; and (3) the biobank gains approval from a national ethics committee and the national authority in charge of data protection.[134] This major exception creates, in essence, blanket consent for subsequent uses rather than truly requiring informed consent by the individual. Withdrawal of information can be requested by the individual, but any results already obtained by use of the sample will not be destroyed.[135]

Estonia takes a different approach and requires informed consent for participation in the national genetic database. Individuals must sign a consent form after going through counseling sessions on the EGP.[136] The consent form, though, supplies information on the EGP only to the extent necessary to foster an informed decision on whether to donate a sample.[137] This broad consent incorporates subsequent uses.[138] Estonia does not attempt an ongoing consent process for each distinct research use.[139] Estonia does allow the individual to withdraw consent until the tissue samples or health data are encoded.[140] This may be somewhat of a

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129 Cardinal & Deschênes, *supra* note 30, at 47.
130 *See supra* notes 28–29 and accompanying text.
131 Cardinal & Deschênes, *supra* note 30, at 47.
132 *Id.* at 49.
133 *Id.*
134 *Id.*
135 Anderlik & Rothstein, *supra* note 56, at 411.
136 Gibbons et al., *supra* note 15, at 112.
137 *Id.*
138 *Id.* "The Estonian Genome Research Project is based on a very broad description of the project as a basis for consent." *Id.*
139 *Id.* Additional uses of the data must be disclosed at the beginning but not thereafter. *Id.*
140 Hsieh, *supra* note 73, at 382.

hollow right, however, since the data processor encodes the information as soon as possible after collection.[141] After encryption of the data, the donor may request destruction of the key that would enable decoding of the information.[142] The EGP can still use the genetic sample and the health data, but it would be impossible to connect that data to an individual.[143]

The UK project also seeks blanket informed consent that covers subsequent uses of the genetic sample. UK Biobank states that "[b]ecause it will be impossible to anticipate all future uses, consent will be sought for research in general that is consistent with UK Biobank's stated purpose (rather than for specific research)," though "[f]urther consent will be sought for any proposed activities that do not fall within the existing consent."[144] Essentially, if a future use does not fall within UK Biobank's broadly stated goal—"to build a major resource that can support a diverse range of research intended to improve the prevention, diagnosis, and treatment of illness and the promotion of health throughout society"[145]—then future consent will be sought. The last part of the stated goal, promotion of health, is so broad that a subsequent legal use of genetic samples that falls outside of that objective is difficult to imagine. Participants may withdraw from UK Biobank at any time without explanation or penalty.[146]

In the United States, the Common Rule on Protection of Human Subjects ("Common Rule") governs human subjects research.[147] The DHHS devised the Common Rule to safeguard the rights of human research subjects; it "applies to all non-exempt research conducted by or supported by [several] federal agencies."[148] A national biobank supported by the DHHS, for instance, would fall under this rule, which requires informed consent by the individual for each research project.[149] Presumably, then, blanket consent would not be acceptable under the Common Rule. A genetic biobank, however, may seek to circumvent this regulation by claiming that its activities do not constitute human

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141 *Id.*

142 Cardinal & Deschênes, *supra* note 30, at 49.

143 *Id.*

144 UK BIOBANK, *supra* note 90, at 5–6.

145 *Id.* at 3.

146 McHale, *supra* note 7, at 85.

147 LOWRANCE, *supra* note 67, at 3; *see also* Basic HHS Policy for Protection of Human Research Subjects, 45 C.F.R. § 46.101–46.124 (2010) (detailing the Common Rule as applied to the Department of Health and Human Services).

148 Jennifer Girod & Katherine Drabiak, *A Proposal for Comprehensive Biobank Research Laws to Promote Transnational Medicine in Indiana*, 5 IND. HEALTH L. REV. 217, 220 (2008).

149 45 C.F.R. § 46.116.

subjects research as defined by the Common Rule.[150] The regulation states the following:

> (b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:
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> . . . .
>
> (4) Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, . . . if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.[151]

The first collection of data would be covered by the Common Rule,[152] but subsequent uses that rely on existing data, such as biological samples stored in a biobank, appear to be exempted from the Common Rule's protections. In fact, OHRP explicitly states that it does not consider research performed on coded private information or specimens to involve human subjects as defined by the Common Rule when two conditions are met:

> (1) the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
>
> (2) the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example: [regulations are in place to separate the code key from the researchers].[153]

Some scholars argue that this guidance should not apply to genetic biobanks because investigators could always "readily ascertain the

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150 Greely, *Genomic Biobanks*, *supra* note 16, at 353.
151 45 C.F.R. § 46.101(b)(4).
152 *Id.* § 46.102(f).
153 OHRP, *supra* note 94, at 3–4.

identity" of participants via characteristics of their genetic sample.[154] For instance, the investigator could request updated information on a sample that is particularly distinctive of the person, forcing the biobank to contact the individual participant and potentially reveal the identity to a researcher. As written, however, the OHRP guidelines appear to contemplate a genetic biobank and specifically exempt such institutions from the informed consent requirements of the Common Rule for any subsequent research uses.[155]

The notion of informed consent is firmly embraced by common law and American tort law, and the Supreme Court has affirmed this principle, saying that "[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body."[156] Performing a medical procedure on an individual without informed consent could result in a tort of common law battery.[157] This doctrine, however, would likely apply only to the initial taking of the genetic sample when a health care worker would have to come into physical contact with the donor. Physical force to the body of another is the touchstone of a common law battery.[158] An individual may also have a colorable Fourth Amendment claim against unwarranted search and seizure if genetic samples are taken without informed consent.[159] The Supreme Court has stated, "The basic purpose of [the Fourth] Amendment, as recognized in countless decisions of this Court, is to safeguard the privacy and security of individuals against arbitrary invasions by government officials."[160] The taking of a genetic sample and the subsequent testing of that sample without permission by the individual would likely be deemed an illegal search under Supreme Court doctrine.[161] The text of the Fourth Amendment, though, only

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154 Greely, *Genomic Biobanks*, *supra* note 16, at 354–55.

155 *Id*. at 355–56. The ethics of such a maneuver are certainly up for debate. *Id*. at 356. In addition, the Health Insurance Portability and Accountability Act ("HIPAA") may prevent the future link to medical records without continued authorization, though this position is also up for debate. *See* Rothstein, *supra* note 52, at 93–94.

156 Cruzan v. Dir., Mo. Dep't of Health, 497 U.S. 261, 269 (1990) (quoting Schloendorff v. Soc'y of N.Y. Hosp., 105 N.E. 92, 93 (N.Y. 1914)).

157 *See* Canterbury v. Spence, 464 F.2d 772, 783 (D.C. Cir. 1972) (allowing a case to reach the jury in which a youth submitted to a back surgery without being adequately informed of the risks).

158 BLACK'S LAW DICTIONARY 173 (9th ed. 2009).

159 *See* U.S. CONST. amend. IV ("The right of the people to be secure in their persons, houses, papers, and effects, against unreasonable searches and seizures, shall not be violated . . . .").

160 Camara v. Mun. Court of San Francisco, 387 U.S. 523, 528 (1967).

161 *See* Skinner v. Ry. Labor Execs. Ass'n, 489 U.S. 602, 616–19 (1989) ("[T]he permissibility of a particular practice 'is judged by balancing its intrusion on the individual's Fourth Amendment interests against its promotion of legitimate governmental

protects against unreasonable searches; therefore, a court would attempt to determine whether the taking of the genetic sample was unreasonable by using the balancing test set forth in *Skinner v. Railway Labor Executives Ass'n*—"the permissibility of the search 'is judged by balancing its intrusion on the individual's Fourth Amendment interests against its promotion of legitimate governmental interests.'"[162]

Skinner upheld a search of railway employees for alcohol and drugs in the blood because of the employees' diminished expectations of privacy in such a heavily regulated industry and the safety concerns at issue.[163] Those concerns would not be present for a genetic biobank for a few reasons. First, the holding in *Skinner* rested in part on the operational realities of the workplace; accidents in the railway industry can seriously harm the public, but drug and alcohol testing can provide a safeguard.[164] Second, the Court stressed the diminished expectations of privacy inherent in such a heavily regulated industry.[165] In contrast, the Fourth Amendment and various privacy statutes create the opposite expectation for U.S. citizens. An average U.S. citizen would have no lowered expectation of privacy when using a genetic biobank.

In other cases, the Court affirmed that such a search without individualized suspicion is only permissible in limited circumstances, such as border checkpoints, sobriety checkpoints, and administrative inspections in closely regulated businesses.[166] The research interests that are pervasive in a genetic biobank should not tip the balance of reasonableness in favor of the government either. Research does not have the same import as safety on a railroad; though public health may be helped in the long run, research does not have the immediate impact of, for example, ensuring railroad engineers are not drunk on the job.

The Common Rule and Supreme Court precedent require informed consent by the individual for at least the initial donation of the genetic sample. Subsequent uses of the sample, however, may not require separate consent of the individual. A claim could be made that subsequent uses qualify as unreasonable searches under the Fourth Amendment, because such testing could reveal new information about the donor. As noted above, the Supreme Court has recognized

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interests.'" (quoting Delaware v. Prouse, 440 U.S. 648, 654 (1979))); *see also* United States v. Martinez-Fuerte, 428 U.S. 543, 555 (1976) (weighing government searches against the individual's Fourth Amendment interests).

162 *Skinner*, 489 U.S. at 619 (quoting *Prouse*, 440 U.S. at 654) (internal quotations omitted).

163 *Id.* at 624–25.

164 *Id.* at 628–30.

165 *Id.* at 627.

166 *See*, *e.g.*, Chandler v. Miller, 520 U.S. 305, 308 (1997) (citing cases upholding the limited right to conduct searches "without grounds for suspicion").

subsequent testing as a separate search from the initial collection. In that case, however, the balancing of harms may look quite different. For one thing, the individual's expectation of privacy must be lower because the person must have already consented to donating the genetic sample to a biobank. That consent would presumably include a statement of possible future research. Furthermore, the additional harm to the person would possibly be lower than the harm of extracting a genetic sample in the first instance. While a future study may reveal one more gene or condition, the initial taking of the genetic sample could possibly reveal a litany of conditions in the individual, including drug use, sexually transmitted infections, or a variety of genetic conditions.

C. Feedback of Clinically Significant Information

Traditional public health screening programs, like those for cardiovascular issues, are intended to encourage people to obtain medical care to prevent or treat disease. Indeed, they serve little purpose without a connection to medical care.[167] Similarly, a genetic biobank may produce great advances in biomedical research, but it would not protect the interests of participants without a connection to individualized care.[168] For example, consider a woman participant in a national biobank whose genetic analysis turned up a deleterious BRCA1 gene. Inheritance of a harmful mutation in BRCA1 significantly increases a woman's risk of developing breast or ovarian cancer; some estimates predict that sixty percent of women who carry a BRCA1 gene mutation will develop breast cancer at some point in their lives, compared to rates as low as twelve percent of women in the general population who do not have the BRCA1 genetic mutation.[169] Disclosure of the genetic test may allow the woman to stave off the worst consequences of breast cancer through early detection programs or preventative measures.

A genetic biobank must balance this benefit of disclosure with two competing concerns. First, an individual has the right *not* to know. A woman may wish to live in ignorance of a medical condition rather than

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[167] *See* Wendy K. Mariner, *Public Health and Law: Past and Future Vision*, 28 J. HEALTH POL. POL'Y & L. 525, 534–35 (2003) ("[Public health screening programs] serve little purpose without links to medical treatment.").

[168] Many patients may expect feedback of clinically significant information or even small, incremental risks. Jasper Bovenberg et al., *Biobank Research: Reporting Results to Individual Participants*, 16 EUR. J. HEALTH L. 229, 237 (2009).

[169] *BRCA1 and BRCA2: Cancer Risk and Genetic Testing*, NAT'L CANCER INST. (May 29, 2009), http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA.

live with the known increased risk of breast cancer weighing on her.[170] The Universal Declaration on the Human Genome and Human Rights supports this right not to know; it states that "[t]he right of each individual to decide whether *or not to be informed* of the results of genetic examination and the resulting consequences should be respected."[171] Second, genetic tests reveal information about third parties who may not be participating in the biobank and do not wish to know or have others know about their medical conditions. Thus, a genetic biobank must choose to balance between the benefit of revealing information and the harm to third parties and willfully ignorant participants.

Of the countries studied in this Article, only Estonia provides a mechanism for feedback of clinically significant information to reach the individual donor.[172] Iceland's HSD Act makes no mention of receiving feedback. An Icelander can obtain certain processing information, but that right is qualified if the person's right is deemed subordinate to other interests, including the interests of others.[173] Similarly, UK Biobank only provides feedback to consenting patients "on measures taken at the physical assessment."[174] It "will not provide participants with information (genetic or otherwise) about their own individual results derived from examination of the database or samples by research undertaken after enrolment."[175] Estonia, though, gives feedback to gene donors who affirmatively request such information.[176] This protects the right not to know, but it does not completely fulfill any duty to provide clinically significant information because the gene donor must actively request the information. Estonia's EGP does not seek out donors who would benefit from personal genetic information.

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170 Anne Maria Skrikerud, *Information Rights on the Edge of Ignorance*, *in* THE ETHICS OF RESEARCH BIOBANKING 49, 54 (Jan Helge Solbakk, Søren Holm & Bjørn Hofmann eds., 2009). The right could be considered either the liberty to refrain from being informed or the right to ignorance. *Id.* The former puts the burden on the individual to avoid information, while the latter puts the burden on the biobank not to inform. *Id.* For purposes of this Article, the right not to know deals with actions by the biobank.

171 Universal Declaration on the Human Genome and Human Rights, UNESCO Gen. Conf. Res. 29 C/Res. 16, *reprinted in* Records of the General Conference, UNESCO, 29th Sess., 29 C/Res. 19, at 41 (1997) (adopted by the UN General Assembly, G.A. Res. 152, U.N. GAOR, 53rd Sess., U.N. Doc. A/RES/53/152 (1999)) (emphasis added), *available at* http://unesdoc.unesco.org/images/0011/001102/110220e.pdf#page=47.

172 Gibbons et al., *supra* note 15, at 124.

173 Hsieh, *supra* note 73, at 393.

174 Carolyn Johnston & Jane Kaye, *Does the UK Biobank Have a Legal Obligation to Feedback Individual Findings to Participants?*, 12 MED. L. REV. 239, 239 (2004).

175 UK BIOBANK, *supra* note 90, at 8. British legal holdings may supply a duty to warn to UK Biobank. Johnston & Kaye, *supra* note 174, at 246.

176 *Main provisions*, *supra* note 85.

The U.S. regime, however, may be more complicated if a genetic biobank draws on the clinical physician's experience of a duty to warn. This duty has been discussed in various state courts, but no federal holding guides the decisions. In 1996, a New Jersey court held in *Safer v. Estate of Pack* that physicians have a duty to warn against foreseeable risks that can be eliminated or mitigated by timely intervention.[177] In that case, a physician failed to warn a daughter that her father was diagnosed with hereditary colonic polyps that could lead to cancer. Forty years after the father's diagnosis, the daughter sued the physician for failing to warn her of the risk.[178] *Safer* explicitly rejected a Florida case that held that physicians only had a duty to warn their patients and not third parties who may be affected by the genetic disorder.[179] Treating physicians do not escape this duty when they also act as researchers.[180]

These cases, though, all deal with treating physicians who have direct and ongoing contact with the patient and related third parties. While it has been suggested that researchers who are not treating physicians may owe a similar duty to warn,[181] no case has firmly established that principle. The U.S. National Bioethics Advisory Committee advises that disclosure of research results to participants should be an exceptional circumstance and occur only under the following three conditions: "(1) the findings are scientifically valid and confirmed, (2) the findings have significant implications for the participant's health concerns, and (3) a course of action to ameliorate or treat these concerns is readily available."[182] This would impose a duty to warn on researchers for certain conditions, such as a deleterious BRCA1 gene, but not others for which the science is questionable or no therapy yet exists. Although this canon may produce the benefits of feedback in some instances, it creates a nebulous standard for researchers who must decide whether the science is clear or a valid treatment is available. What level of consensus in the scientific community is necessary for a finding to be valid? What constitutes a valid treatment? And to whom must the treatment be available? These questions have not yet been answered, but would be critical in determining the appropriate standard for feedback of clinically significant information found by a biobank.

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177 677 A.2d 1188, 1192 (N.J. Super. Ct. App. Div. 1996).

178 *Id.* at 1189–90.

179 *See id*. at 1192–93 (declining to follow the Florida Supreme Court's holding in *Pate v. Threlkel*, 661 So. 2d 278, 282 (Fla. 1995)).

180 Moore v. Regents of Univ. of Cal., 793 P.2d 479, 485–86 (Cal. 1990).

181 Grimes v. Kennedy Krieger Inst., Inc., 782 A.2d 807, 836 (Md. 2001).

182 McHale, *supra* note 7, at 91.

IV. STRUCTURE OF A POSSIBLE BIOBANK FOR THE UNITED STATES

The experiences of Iceland, Estonia, and the United Kingdom in establishing a national genetic database can provide important lessons on privacy and confidentiality, informed consent, and feedback of clinically significant information for a potential genetic biobank for the United States, which must also be conscious of the existing regulatory and legal framework. With that foundation in mind, this Part will explore the potential structure of a U.S. genetic biobank.[183]

All three international biobanks utilize some type of coding technique.[184] The leading alternative—anonymization—leads to a much less scientifically useful biobank because researchers cannot utilize updated information. Iceland, Estonia, and the United Kingdom recognized this limitation and implemented a key code system to protect confidential medical information, but still allow for an active biobank. Estonia adds an extra layer of security by using a double coding system that separates personal information from medical and genetic data. U.S. regulations from OHRP offer the same conclusion as the international databases: information should be coded rather than anonymized. This provides the best balance between privacy and usefulness. Furthermore, U.S. legal doctrine protects against illegal breaches of privacy. Individuals have a privacy right in protecting the confidentiality of important medical information.

Therefore, a U.S. biobank should utilize a coding system. Taking Estonia's double coding system one step further, the U.S. database should use a triple coding system, as shown in Figure 1.[185] This system will protect against unscrupulous individuals matching up health and personal data with the genetic sample but still allow researchers to use updated demographic and environmental data throughout the life of the biobank.

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[183] This will focus on a biobank with some government involvement. Wholly private companies could also create large research databases using volunteers. They would face many of the same issues presented in this Article, excluding, for example, the Fourth Amendment issue of unwarranted search and seizure due to lack of state action.

[184] *See supra* Part III.A (discussing confidentiality and privacy issues).

[185] The United States biobank would contain three different codes, represented in Figure 1 by the keys necessary to undo the coding: a genetic key, a clinical key, and a master key. The coding system thus provides three levels of protection, rather than the two codes given in Estonia.

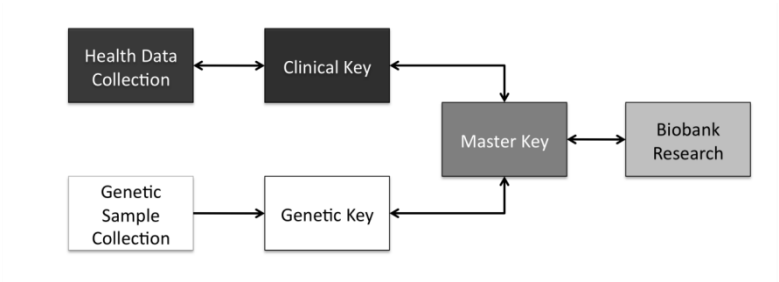

Figure 1. The triple coding system would provide heightened protection of all data.

The coding system process would be conducted as follows. First, health data would be collected by a healthcare worker. This data would then be passed to a processor to assign a random sixteen-digit key to the data. Health data collection is an ongoing process, as shown by the double arrows in Figure 1. This allows the information to be regularly updated, which is one of the advantages that the coding system provides over complete anonymization.

Second, a trained biobank technician collects a genetic sample from the donor. To maintain confidentiality for the donor, the technician would not be the same person as the health data collector; the technician would not know any of the donor's health data. The genetic sample would then be passed to a processor to assign it a sixteen-digit key distinct from the health data key. With two separate keys, an individual who possesses the genetic key still cannot connect the genetic sample to a donor's health data. Similarly, an individual who decodes the clinical key cannot connect that data to a specific genetic sample.

Third, each processor (clinical and genetic) sends the encrypted data to a master processor who links the two codes with a master code, a third unique sixteen-digit code. The master processor holds the master key—the only key that can connect genetic samples to health data. The master key will be kept in a highly secure database controlled by a select number of processors. This ensures that few eyes can view the data. All master processors will be under confidentiality oaths and threatened with criminal sanctions for a violation. If a breach does occur, the number of possible culprits will be small, likely leading to immediate sanctions and restitution for the victim.

Researchers at the biobank receive health and genetic data coupled together under the master code. They can request updates to the health and environmental data, as shown by the double arrows from the biobank back to the health data collection, but this request must go

through the master key and clinical key to ensure confidentiality. No coding system can ensure that researchers will not deviously request highly specific information in an attempt to ascertain the identity of a genetic sample, but the U.S. legal system should supply the necessary protection for unnecessary infringements of privacy.[186] Such unwarranted invasions would certainly fail the *Westinghouse* factors: there is no research need for access to the personal information; the type of record sought has no bearing on research purposes; the potential harm is a constitutional violation of the right to privacy of sensitive medical information; disclosure could harm the relationship between the general population and the biobank if the public loses trust in the biobank and refuses to provide additional data; and an express statutory mandate, or at least an articulated public policy, requires that such information remain private.[187] A researcher who seeks out such information should be punished, and the victim should receive compensation. The U.S. legal system buttresses a coding system to promote privacy of all information collected by the biobank.

A genetic biobank may test the boundaries of informed consent, as evidenced by the presumed consent model of Iceland and the blanket consent prevalent in Estonia and the United Kingdom.[188] Presumed consent, while making the work of a biobank easier, suffered from such a backlash in Iceland that the licensee, deCode, decided to seek informed consent on its own. Informed consent, though, does not truly appear to be completely informed consent for a biobank. Rather, informed consent has become blanket consent. For example, Estonia only seeks informed consent on the issue of whether the participant wishes to donate in the first instance; the participant does not give informed consent each time the sample is used for a new and distinct research purpose. The exigencies of a biobank have created this warping of informed consent because future uses of the data cannot be anticipated at the time of collection. It would be prohibitively expensive to build a biobank for one research project and equally ineffective to seek out consent for each individual study. The OHRP guidelines seem to accept this reality by requiring informed consent only for the initial collection of data and blanket consent for subsequent uses. The Supreme Court may require

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[186] *See supra* text accompanying notes 96–104 (identifying case law discussing the constitutional right of privacy).

[187] *See supra* text accompanying note 104 (listing the *Westinghouse* factors). *Cf.* United States v. Westinghouse Elec. Corp., 638 F.2d 570, 578 (3d Cir. 1980) (delineating factors to determine whether privacy rights have been infringed);.

[188] *See supra* Part III.B (discussing informed consent and humans as research subjects).

extra protection, but it is not clear that subsequent research without traditional informed consent would fail the balancing test of *Skinner*.[189]

A U.S. biobank, however, can work with the realities of the situation and attempt to include informed consent as an ongoing process rather than marginalize it as blanket consent at the outset. Participants in the U.S. biobank should be given biannual updates of the research at the biobank, including current and proposed future studies and the eventual uses of that research. Each donor must then affirmatively elect to remain in the biobank by signing a written authorization form included in the biobank update. The active decision to remain in the biobank is key to not allowing informed consent to become presumed consent. This also allows the participant the option to withdraw, maintaining donor autonomy in the process. This ongoing informed consent process should strike an appropriate balance between protecting donors as human research subjects and allowing a biobank to operate as planned. Future research projects can continue without cost- and time-prohibitive consent for each study. At the same time, donors must actively choose to continue participation in the biobank; their consent cannot be presumed in the absence of an affirmative withdrawal.

Finally, the U.S. biobank must meet the challenge of providing feedback of clinically significant information despite a nebulous legal mandate from state courts.[190] Iceland and the United Kingdom both avoid the issue by refusing to provide feedback. Specifically, UK Biobank will provide the usual clinical information to the donor, much like any routine doctor visit, but the donor will never receive individualized feedback from the genetic studies.[191] The participant will not learn of genetic predispositions from UK Biobank. In Estonia, the donor must actively seek out the information; researchers at EGP will not initiate the feedback.[192] The situation of biobanks is further complicated by the corollary right not to know—the donor may wish to live in blissful ignorance of any genetic factor that could lead to disease. In the United States, any duty to warn imposed by courts or advised by bioethics committees appears to hinge on the validity of the science, the

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189 *See supra* text accompanying note 162 (describing the *Skinner* test as "balancing [the] intrusion on the individual's Fourth Amendment interests against [the] promotion of legitimate governmental interests").

190 *See supra* Part III.C (discussing issues related to feedback of clinically significant information).

191 *See supra* notes 174–75 and accompanying text (discussing UK Biobank's mechanism for feedback of clinically significant information).

192 *See supra* note 176 and accompanying text (explaining Estonia's mechanism for feedback).

foreseeability of the victim, and the availability of treatment.[193] Unfortunately, genetic research is not so straightforward at this time to create bright line legal rules for researchers. In addition, it is not clear that a researcher who is not also the treating physician has a legal responsibility to provide this feedback.

Until those legal questions are solved, the U.S. biobank should not place the burden on the researcher to provide immediate feedback on clinically significant information. Instead, the United States should adopt a hybrid system that crosses the UK and Estonian regimes. For clinical information, the participant should receive feedback on abnormal results—such as the UK Biobank provides. This fulfills the requirements of most jurisdictions that impose a duty to warn. The treating physician or healthcare worker who collects health data from the individual is acting as a treating physician; they come into personal contact with the donor and can provide traditional medical aid. For genetic data, the Estonian regime should guide the U.S. biobank policy. Donors must actively seek out their own information from the biobank. This accomplishes two aims. First, the right not to know can be protected. The donor can either choose to know of a genetic risk or live in ignorance. Second, researchers will not have to entangle themselves in the unclear legal doctrines that currently surround a duty to warn of genetic risk. The onus would be on the donor to seek out the genetic information.

This balance could be reversed, however, by stricter regulations from DHHS that clearly define which genetic risks should be communicated to donors. For example, if the DHHS determines that knowledge of a deleterious BRCA1 gene would be clinically useful and significant information for a donor, regulations on the biobank could require such information to be passed back to a donor. Rather than force each researcher to determine whether the findings are scientifically valid or whether a treatment for the genetic risk is available, a national body of scientists can review current genetic knowledge and create uniform standards. The right not to know this information could be protected by explicit refusal to know of genetic risks by the donor. For instance, in the informed consent process, the donor could make it clear that he does not want to learn of the genetic risks that may be uncovered by the biobank. Those who want to learn of the risks can benefit from feedback of clinically significant information, while those who wish to remain in ignorance can employ the right not to know.

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193 *See supra* notes 177–81 (discussing state case law in the United States).

V. CONCLUSION

Before the United States implements a national biobank, public fears over misuse of genetic information must be calmed. Focusing on privacy and confidentiality, informed consent, and feedback of clinically significant information can begin to alleviate concerns by providing a solid ethical and legal framework that protects individual donors from misappropriation of genetic and health data. The biobanks of Iceland, Estonia, and the United Kingdom all provide important lessons for a domestic database as the United States steps boldly into a "brave new world."