REPORT

On genetic data in private insurance

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Disclosure to insurers of the results of genetic testing by the insured or by insurance applicants has become a topic of considerable interest in recent years. The reason is that a person's genetic data is associated with their predisposition to develop certain serious diseases which is seen by some as critical in the context of life or health insurance. The issue maintains its relevance due to constant breakthroughs in genetics and the decoding of the human genome, especially with regards to association of mutations or genetic markers of specific genes with manifestation of disease.

With a previous recommendation on "Genetic Data" the Commission already raised a number of related ethical, legal and social questions. At the core lies the concern about an eventual establishment of some form of favourable or unfavourable "genetic discrimination" in insurance depending on whether the insured have a genetic predisposition for a disease or not. Two questions emerge in this respect: a) to what extent is this concern justified considering the real predictive value of genetic markers, and, b) what are the arguments for and against a statutory regulation of the use of genetic date in insurance.

The present report attempts to analyse these questions in preparation of a Commission's Recommendation. The first chapter discusses the issue of the predictive value of genetic data providing examples of diseases. The second chapter examines the relevant ethical problems. The third chapter outlines the legal dimension of the issue since by now special laws have been put in place in some cases.

1. GENETIC TESTING AND PREDICTION OF GENETIC DISEASES

A. Introduction

In 1999, the Task Force for Genetic Testing came down to the following definition of genetic:

Any *"…analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes"* (Burke W, 2002 and Holtzman NA and Watson MS, 1999).

This definition is quite broad and allows for different interpretations. With the advance of genetics, in particular, the limits are shifting. In the US Bill of Law GINA on genetic discrimination (Genetic Information Non-discrimination Act, see 3B), non-genetic tests are specified explicitly as: "an analysis of protein or metabolite that does not detect genotypes, mutations or chromosomal changes" or is "directly related to a manifested disease, disorder or pathological condition that could reasonably be detected

by a health care professional with appropriate training and expertise in the field of medicine involved". Based on the definition of genetic testing, personal genetic information is the information that is generated by genetic testing. However, here as well the limits are unclear as some authors, for instance the GINA Bill of Law, include in an individual's genetic information data from genetic testing and the manifestation of genetic diseases in family members.

Genetic testing is carried out for a variety of reasons such as the diagnosis of an already manifested disease, prenatal control or to determine genetic predisposition to specific disorders. The first two applications are not relevant to this report. Here, we are interested in genetic testing that identifies increased risk of disease manifestation in healthy, asymptomatic individuals. Genetic tests are also extremely useful in pharmacogenetics and in personalized medicine[1].

Genetic and environmental factors interact in the development of disease by creating a spectrum (Figure 1), with the so-called genetic or hereditary diseases associated with exclusively genetic causes (like β-thalassaemia) at the one end and diseases with exclusively environmental (external) causes (like trauma) at the other end. The causes of most human pathological conditions, however, lie somewhere in-between, i.e. it is a combination of genetic and environmental factors that leads to manifestation of disease, such as diabetes or cardiovascular diseases.

Depending on their genetic basis, genetic diseases are divided in (i) single-gene[2], (ii) polygenic[3], and, (iii) mitochondrial[4] (Human Genome Project Information[5]). A gene's disease-causing mutation is either dominant or recessive if one or two mutated alleles are required respectively for the manifestation of the disease. Finally, the likelihood of disease depends on the *penetrance*[6] of the allele. The evaluation of the results of a genetic test depends directly on the category of genetic disease for which the test is taken. In general, the evaluation of genetic testing results for single-gene diseases is simpler as compared with multifactorial diseases.

The genetic disorders relevant to the present report are those manifested after an application for insurance has been made, so usually after infancy. Genetic tests potentially of value to health and life insurance are those that can contribute to determining the insured risk, i.e. those able to detect mutations which are well-documented to be associated with a specific disease(s) and their penetrance is known so that, based on the outcome of the genetic test, it is possible to determine the likelihood of manifestation of the disease.

According to the reliable network GeneTests, as of today (data accurate on 4/10/2007) there are 1.175 genetic tests in clinical use and 282 at the experimental stage

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[1] See par. 1(C): The value of genetic information for personal health and scientific progress and the potential of genetic testing.

[2] They are caused by the disease-causing mutation of a single gene, e.g. Huntington's chorea, cystic fibrosis, Marfan's syndrome, etc.

[3] More than one genes are involved in the manifestation of the disease, e.g. Alzheimer's disease, diabetes, arthritis, etc.

[4] Mutations in the non-chromosomal DNA of the mitochondria.

[5] http://www.ornl.gov/sci/techresources/Human_Genome/home.html

[6] Penetrance is complete if all the carriers of disease-causing alleles will manifest the disease or incomplete when only some of the carriers will develop the disease.

for 1.475 diseases. NCBI's on-line database Genes and Disease[7] provides information on the association of one or more genes with 84 groups of diseases (Table 1), whereas there are overall more than 6000 single-gene disorders that affect approximately 1/200 births (Human Genome Project Information). Of the available genetic tests, those with predictive value concern 61 diseases as a whole. Table 2 provides selective information on some of the most common diseases. The available genetic tests that qualify as predictive are further classified according to the penetrance of the disease causing mutations into presymptomatic and predisposition tests (McPherson E, 2006).

The first category comprises tests that detect mutations with complete penetrance, where the manifestation of disease is certain for the carriers of disease-causing mutations, e.g. the genetic test for Huntington Disease. The second category includes tests that detect mutations with incomplete penetrance. The carriers of such mutations will not necessarily develop the disease but their chances are increased compared to the general population. Tests for cancer belong to this category. In this case, if the result is positive, medical testing will need to be carried out more frequently in the future; if negative, the likelihood of disease is the same with that of the general population, but not zero. Below, we provide some examples of genetic tests from both categories.

i. Huntington Disease

Huntington's disease is a neurodegenerative condition affecting 3-7/100.000 people in western European populations (except among the Finns). The incidence is significantly lower in Japan, China and black Africans (Warby, Graham and Hayden, table 2). The HD (IT15) gene is involved in this condition and the disease is inherited in an autosomal[8] and dominant manner. The available genetic test detects the alleles of gene HD[9] in the person undergoing the test.

In the case of Huntington's disease, genetic testing can answer with near certainty to whether someone, with relevant family history, will develop the disease or not. The available genetic test detects the disease-causing alleles with an accuracy of 100%. However, it cannot predict with certainty the time of disease onset. Since there is currently no treatment for this condition, identifying someone as a carrier has no prophylactic value.

ii. Early Onset Familial Alzheimer, EOFAD

The early onset Alzheimer, like common Alzheimer, is a form of slow-progressing dementia, manifested prior to the age of 65 and represents less than 3% of all Alzheimer cases (Bird, 2007, table 2). The genetic association for the disease seems strong since, of all the early onset Alzheimer cases, 61% of patients have relevant family history and 13%

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[7] On-line database which collects information on genetic testing and is funded by the American National Institutes of Health (NIH's) http://www.ncbi.nlm.nih.gov/

[8] The responsible gene for the disease is situated in an autosomal, not a sexual, chromosome. Therefore, there is no difference in heredity between the sexes. See report on genetic data.

[9] The test is based on DNA analysis with the PCR or the Southern hybridization method and the number of repeats in a nucleotide triplet. The penetrance of the allele depends on the number of repeats. HD alleles are classified into three categories: normal, intermediate and HD-causing.

have relatives in three generations that developed the disease. Early onset Alzheimer is manifested in 41.2/100.000 people aged 40-59.

The involvement of three genes has been identified, PSEN1, PSEN2, APP (table 2). In all EOFAD cases heredity is autosomal and dominant. Genetic tests have been developed and are used clinically to detect disease-causing mutations for all three genes. The highest numbers of positive scores in EOFAD patients are achieved by tests detecting mutations in the PSEN1 gene. The evaluation of genetic tests for EOFAD is not as simple as in the test for Huntington's disease since the available tests do not detect all the mutations and in some patients the test yields a negative score. Nevertheless, penetrance of PSEN1 gene (AD3) mutations is complete whereas penetrance of PSEN2 (AD4) mutations is 95%, i.e. if one of the disease-causing mutations is identified in a healthy subject the manifestation of the disease is almost certain.

iii. BRCA1 and BRCA2 Hereditary Breast/Ovarian Cancer

Mutations in BRCA1 and BRCA2 genes have been found to predispose for breast, ovarian, prostate and other cancers (Pertucelli et al., 2007, table 2). There are genetic tests that detect mutations in these genes but the reliability of the test and the evaluation of the results are complex, more so than in the case of EOFAD mentioned above. Due to a multitude of disease-causing mutations for both genes, there is no single test capable of detecting all of them.

For a healthy individual with a family history of this category of cancers it is important to know which mutation occurred in those family members that developed cancer. Calculation of the penetrance of the mutations of genes BRCA1 and BRCA2 is not a simple task, as different mutations have different penetrance and the likelihood of cancer varies in different age groups. For example, the probability of breast cancer in BRCA1 mutations ranges from 3,2% (at the age of 30) to 85% (at the age of 70). The probability is similar for BRCA2 mutations.

The likelihood of ovarian cancer is lower. The availability of several calculation models for the probability of cancer in case disease-causing mutations are detected, which vary significantly in their predictions, is a sign of the complexity of the evaluation of the test results. Another important factor is that a negative score in the genetic test does not mean that the subject will not develop the specific cancers, only that the risk is not higher as compared with the general population. Finally, a positive score in a healthy subject practically means that the person in question must undergo more frequent examinations but it makes no difference in terms of treatment if cancer does occur.

In brief, testing for BRCA1/2 gene mutations is complicated and great caution is required in the choice of the detection method as well as in the evaluation of the result.

In conclusion, although most genetic tests cannot predict the manifestation of a genetic disease with certainty, they have considerable prophylactic value for the person undergoing the test. By identifying a predisposition for cancer, for example, one can be protected by regular medical examinations for early identification and treatment of tumors. It is well documented that early diagnosis saves lives in such situations.

B. Genetic testing laboratories

There are at least 611 certified genetic laboratories worldwide that are registered with the reliable network GeneTest. Greece has one certified genetic laboratory[10]. However, other public or private laboratories carry out genetic tests without ISO certification, as there is no law regulating the operation of non-certified laboratories[11].

The multiplication of new genetic tests, the increase in genetic laboratory numbers (figure 2) and the widespread application of genetics in medicine create an urgent need to ensure the quality of services offered by genetic laboratories. The operation of certified genetic laboratories is governed by international certification rules. Among the requirements for quality control according to relevant ISO regulations are the validity of method, the evaluation of the results by trained professionals and safeguard clauses for the protection of patient rights. With regards to the latter, in particular, the rules for certification require a referral by the treating physician and the consent of the person taking the test following comprehensive information by qualified scientists on the consequences of the test for those involved and their families. The anonymity of samples and the duty of confidentiality of the staff are also ensured. Without certification or some other kind of regulation of lab operation, the validity and protection of the results cannot be guaranteed.

C. The value of genetic information for individual health and scientific progress and the potential of genetic testing

With the development of genetics, especially of pharmacogenomics and personalized genetics, genetic information becomes increasingly important. Personalized genetics and pharmacogenomics help to predict individual sensitivity to environmental factors, individual response or lack of response to a specific treatment or medicine, etc.

Pharmacogenomics exploits the association between the potency of a particular drug and genetic markers to develop genetic tests for more effective diagnosis and treatment (Goldmann BR, 2005). For instance, genetic information can be used to define the appropriate treatment for various cancer types. It is worth noting here that the case of pharmacogenetics is an example where the use of genetic testing is beneficial to both the insured and insurance companies since the appropriate genetic information helps to save time and resources by applying tailor-made treatments based on the outcome of genetic testing. In this case, avoiding a test for fear of refusal of insurance can be detrimental to both the insured and the insurer.

At the moment many genetic applications may look like something of the distant future for everyday medicine but progress is expected to be fast. The funds allocated to research in human genetics reflect the magnitude of expected benefits for public health. It is thus crucial that everybody should be able to enjoy the benefits of scientific progress and people should not be discouraged on non-medical grounds such as fear of exclusion from insurance.

To give an example of the speedy pace of developments, the cost and time required to decode the human genome dropped dramatically in the last 15 years from 4

[10] BioAnalytic-GenoType S.A.

[11] There is a related opinion by the Committee for Genetics to the Ministry for Health on the operation of genetic labs; the Committee met in 2005-2006 for this purpose.

billion to 2 million dollars. An important international effort is underway to further curtail the cost to less than 1,000 dollars[12] to make decoding practically feasible for patients and healthy-individuals. This could lead to important discoveries from the comparative analysis of genomes[13].

Genetic information may revolutionize medical practice and it is important for the public not to be put off from preventive genetic tests that can prove crucial for personal health. Many believe that the eventual use of genetic data in insurance (and at the workplace too) discourages many citizens not only from undergoing testing but also from participating in research, a view shared by the editors of the highly respected scientific review Nature Genetics (editorial, 39:2, Feb 2007) which prompted them to support the GINA Bill, which bars the use of genetic data in insurance. Therefore, it is necessary to keep the public informed about the latest developments in genetics to avoid unfounded fears and also for an informed demand for a fair regulation of the protection of personal genetic data, to avoid discrimination in life and health insurance as well as in other sectors – which fall outside the scope of the present report – like employment.

D. High risk groups for genetic disorders

The development of genetics and of genetic testing for specific diseases has confirmed empirical knowledge about the higher incidence of certain genetic disorders in particular geographic or racial groups. Examples include β-thalassaemia that has a higher incidence in people originating from the Eastern Mediterranean, Africa and Asia[14] and various disorders with a high incidence in descendants of Ashkenazi Jews like the BRCA1/2 breast/ovarian cancer. In fact, there is a genetic test for a whole range of genetic disorders occurring more frequently in Ashkenazi Jews[15].

The development of genetic tests can contribute to early and accurate diagnosis of genetic conditions thus improving the prospects of management or treatment. Notwithstanding the medical benefits, however, there is an increasing risk of discrimination against these racial groups. Examples of such discrimination appeared in the US, for instance, in the '70s when African Americans who were carriers of sickle cell anaemia, i.e. who were heterozygotes and not actually sick, were either deprived of health insurance or charged with higher premiums (Rothenberg KH and Terry SF, 2002 and Andrews L, 1987). Today testing is optional and this case of "genetic" discrimination and stigmatization is used as an example to learn from in the findings of the American GINA Bill of Law. In the future, if no regulation is adopted, there is a risk that individuals

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[12] George Church's team in Harvard University endeavours to decode the genome of 100.000 people in one year at a cost below 1,000 dollars per person. This effort takes place in the context of the Personal Genome Project (http://arep.med.harvard.edu/PGP/). Besides, the X Price Foundation launched the Archon Genomics Competition that will award 10 million dollars to the first team that will decode the complete genome of 100 people in 10 days at less than 1,000 dollars per genome.

[13] We have seen tokens of the potential of this methodology from projects like the so-called "Iceland experiment" where genetic and other medical data of a big chunk of the population is filed into a database managed by the decode company (http://www.decode.com/) following the adoption of special legislation. This data has already led to significant scientific discoveries.

[14] Regions where malaria used to be endemic.

[15] http://www.diagnogene.com/temp.php?page=laboratory&ltest=jew

belonging to high incidence groups for one or more genetic disorders will be required to undergo genetic testing prior to insurance.

E. Genetic discrimination in insurance

There is no clear-cut definition for the term "genetic discrimination" (Geetter, 2002). In insurance "genetic discrimination" means any form of differential treatment of insurance applicants or insured based on their genetic make-up. Practically, discrimination in insurance manifests either with refusal of insurance or with the application of increased premiums. Another form of discrimination is refusal to pay compensation (Pfeffer et al., 2003).

In private health insurance, particularly in individual plans (as opposed to group health plans that are governed by different rules), discrimination based on personal medical history or, generally, on the level of risk that the insured represents for the insurer is admissible. The acceptance of such discrimination emanates from the optional nature of private health insurance, the availability of social security and mainly the assumption that private health insurance is governed by the principle of reciprocity (and not by the principle of social solidarity as in social security systems).

It should be noted at this point that the legislation that regulates private health insurance varies significantly between countries with developed social security systems - such as the majority of European countries- where private insurance plays a subsidiary role, and countries like the US where there is no social security system and, therefore, citizens' needs must be met entirely by private insurance.

With respect to genetic discrimination, three questions are raised:
i) Whether genetic discrimination is currently occurring in health insurance, in our country and internationally,
ii) Whether genetic discrimination is likely to be an issue in the future,
iii) To what extent is genetic discrimination different from medical discrimination, which is admissible as a legitimate basis for the calculation of risk.

There is no data on genetic discrimination in Greece due to lack of related research. International literature reports cases of discrimination (Low et al., 198, Pfeffer et al., 2003) whereas according to some sources the problem of genetic discrimination does not exist at present and represents only a theoretical risk (Hall and Rich, 2000). In actual fact, the identification of genetic discrimination cases is very difficult as is the identification of and access to high risk for discrimination individuals or groups. An additional difficulty for this kind of research is the subjectivity of the evaluation of discrimination as some cases may be misconstrued as discrimination and *vice versa*. Nevertheless, even those who argue that the problem of genetic discrimination is hypothetical, agree that the enactment of prohibitory laws or/and the wider debate on the issue have lead to a prevailing "ethics" against the use of genetic data that come from genetic testing (Hall and Rich, 2000). Another reason for the small number of reported discrimination cases despite the absence of legislation is probably the fact that most genetic tests are relatively recent and their validity has not yet been evaluated by underwriters for practical purposes. Finally, whilst there is some evidence on how genetic data affects insurance prior to the agreement of a contract there has been no consideration

regarding discrimination after contract agreement, for instance, problems with compensation payments.

Whether genetic data should be treated differently from medical data in insurance is an issue widely debated. Some advocates of excluding genetic data from insurance argue that it is unfair to "punish" people for their genetic make up, i.e. for something they cannot change. Others argue that genetic data can be more easily misunderstood or overestimated compared to medical data and this is sufficient grounds to treat it differently (Holm, 2007). By contrast, those who argue that genetic data should be treated in the same way as medical data do not believe that the former have a higher prognostic value nor that they are more personal or sensitive than medical data (Ashcroft, 2007).

No matter what stance one takes on this, an additional issue is how to ensure the appropriate evaluation of genetic information in order to avoid "misplacing" people in categories of high insurance risk on the basis of inadequately understood genetic information. Such genetic discrimination might be introduced, for example, against healthy subjects who are heterozygotic carriers of mutations that result in disease only in homozygotes. As an example we might cite the parents of children suffering from cystic fibrosis who carry the responsible mutation for the disease but are in no risk of developing cystic fibrosis themselves. There have been reports of such "misguided" discrimination in the UK (Law et al., 1998).

2. ETHICAL ISSUES

Genetic testing or disclosure of related results for private insurance purposes raise two very poignant ethical questions:

a) Is disclosure of these results justified as a requirement for insurance considering that a balance must be struck between economic freedom for the insurer and the need to protect the personality of the insured and also the usefulness of these results for the latter?

b) Are there any collective interests, aside from the individual interests of the two parties that should be taken into account in this balancing?

A. Business risk and protection of personality

1. In general, private insurance is a business activity governed by the principle of reciprocity. The basic idea consists in sharing the risk by a group of individuals who are equally likely to suffer damage which would be unaffordable to the individual person: by paying premiums, a large number of insured cover the expenses the insurer will have to bear for the harm suffered by one of the insured in question (and underwritten by the insurer). This idea presupposes that the insurer – just as any other businessman – also assumes part of the risk arising from the occurrence of unpredicted events.

With regards to life and health insurance in particular (including insurance for professional incompetence), the insurer's risk consists in the occurrence of damage from disease or accident to the insured. In these cases, the calculation of the premium by the insurer is based on statistics on the probability of risk in population groups with common characteristics (e.g. sex, age, lifestyle). Such data include information on health, which the insurer requests from the insured. This information consists of the medical history (of the individual and/or their family) and may include new medical tests. The more accurate the information the more accurate the prediction. By contrast, the poorer the information,

the greater the risk for the insurer. In the latter case, if insurance is not wholly unattractive in business terms, the insurer will try to hedge the risk by increasing the premium based on past data for a similar group.

2. But this purely economic calculation does not settle the issue, for life and health insurance cannot be assimilated to just any other commercial service or commodity. The nature of health information requested by the insurer being sensitive personal data, it goes to the core of the personality of the insured. Any illicit disclosure or other processing of this information may, in view of its nature, result in drastic restriction of individual freedoms, even in violation of human value.

Here, we have to enter two caveats, typical of the differentiation between health and other types of information:

i) The "right of ignorance" pertaining to the subject of health information, i.e. a person may not wish to be informed of data concerning his/her health in order to go on with his/her life undisturbed (Nationaler Ethikrat 2007: 28-29). The disclosure of this information to the insurer as a precondition for insurance encroaches upon this right since the applicant is then forced to choose between taking the insurance and exercising this right or, alternatively, to pay higher premiums.

ii) Medical confidentiality, the purpose of which is to keep serious health information confidential vis-à-vis third parties and to avoid placing one's social life at risk. This is indeed the very reason for which medical confidentiality was put in place.

3. With the development of molecular genetics, the potential opened by the decoding of the human genome and the subsequent expansion of genetic applications in medicine, the importance of genetic testing, in particular, has taken on a prominent place in this debate.

It is pointed out by many that, by disclosing genetic data, the opportunities for violation of personality are multiplied. Since, in principle, genetic characteristics do not change, the identification of any predisposition for serious diseases in one's genome (not of an already manifested disease) may result in lifelong "stigmatization" and, ultimately, to unfair social discrimination (Nationaler Ehikrat 2007: 26-27). In insurance, such discrimination can take the form of premium escalation (depending on the identification or not of a genetic predisposition). Thus it might very well be that, in the future, the cost of health care is reduced for those not found to have any predisposition and increased for the rest, or that insurers might even refuse to underwrite certain conditions.

This line of thinking leads to an absolute ban on disclosure of genetic information to insurers and, needless to say, precludes insurers from requiring genetic testing as a condition to a life or health insurance contract.

From the viewpoint of bioethics, the issue here is whether the economic freedom of the insurer puts the principle of equality at risk for the insured or, seen in the opposite, if concealment of genetic data by the insured creates inequality between the parties in the context of freedom of contract.

With regards to the above, it is worth noting the following:

a) From the discussion in the first chapter, we concluded that genetic information actually has little predictive value as to the certainty of disease manifestation. It makes a more accurate prediction about the likelihood of disease but, on the other hand, allows preventive measures to limit this likelihood. The detection of specific mutations in one's genome that are known to be associated with disease, does not mean, in most cases, that the disease will actually be manifested during the life-span of an individual. The only exception is a number of single-gene diseases (e.g. Huntington's chorea).

b) This means that, compared to other medical information, a greater interest from insurers to have access to genetic information is not necessarily justified. Nevertheless, such an interest is widely based on overestimates of the power of genetic data, i.e. on the erroneous perception that has been cultivated, regarding their increased predictive value for the future health of an individual (HGC Minute 2007: 3.3). This is actually a version of "genetic determinism", a popular belief nowadays, which is due to inaccurate information. The consequences of this misleading perception are not to be overlooked: the emergence of unfavourable discrimination against specific population groups based on their genetic traits, in violation of the principle of equality, is seen in this light, as an existing problem.

c) It is a fact that an absolute prohibition of access of insurers to all information, which may be critical for a particular type of insurance contract, can only increase their business risk. First of all, it does not seem fair that health information that is known to the insured should be withheld from the other party (regardless of its worthy protection as sensitive personal data). Besides, it should not escape our attention that such a prohibition may sustain the overrating of genetic information and the related perception of genetic determinism and, on the other hand, the increased risk assumed by insurers may lead them to a generalized reaction of raising premiums at least for those diseases for which a genetic predisposition can be inferred indirectly i.e. without carrying out any genetic testing.

The above three points seem to us to be important for evaluating the interests of the parties to an insurance relationship.

B. A collective interest involved

However, there is an additional dimension to this debate: the protection of health as a collective interest.

The diffuse perception of genetic determinism that inspires concerns about illegitimate uses of genetic information seems to have created a general reluctance among the public to undergo genetic testing for health reasons (Nationaler Ethikrat 2007:30, HGC Minute 2007:3.8).

This trend is noticeable in the US, for example, and there is a risk for both health services and for individual subjects to miss valuable information that may contribute significantly to good health. In clinical trials for new medicines, reluctance against genetic testing has led to an actual reduction in the number of volunteering participants in research in tailor-made drugs (pharmacogenomics) that are thought to be very hopeful for the future of therapeutic medicine.

Consequently, there is a need to take into consideration the real value of genetic information for the protection of health, which is just as valid as any other medical information and, for all intents and purposes, far removed from the pervasive overrated perceptions we noted before. At the end of the day, this need serves a wider social interest. Indeed, failure to use the potential of additional knowledge on health – such as genetic information – for fear that this knowledge may be used for illicit purposes by third parties causes more harm not only to the individual subject but to a more efficient organization of health care in the general population.

3. THE LEGAL DIMENSION

Very few countries have adopted special legislation on the use of genetic data in insurance. As a rule, the issue is governed by the general laws on the protection of personal data in conjunction with insurance law.

A. International Law

Critical from the point of view of international law is the provision of article 11 of the Oviedo Convention pursuant to which:
"Any form of discrimination against a person on grounds of his or her genetic heritage is prohibited."

A similar provision was included in the UNESCO declaration on the Human Genome.

The Oviedo Convention does not preclude genetic testing for "health purposes" (art. 12) but recognizes the right "not –to-be-informed" (art. 10 (2)). Thus, it seems to refrain from taking a stance on the issue.

Protection of the sensitive nature of personal data (with specific provisions on confidentiality) is embedded in the 3rd Protocol to the Oviedo Convention (Greece has not ratified it) whereas a new Protocol is going to rule on genetic testing for health reasons. Neither of these instruments, however, specifically mentions insurance[16].

B. Other Jurisdictions

Some European countries have enacted special prohibitory laws. Notably, Austria, Denmark, Switzerland, Estonia, Lithuania, Luxembourg, Norway, Portugal and Belgium prohibit disclosure of genetic information to insurers whereas Netherlands allows it only if insurance is above a certain amount. Other European countries observe a *moratorium* whereby insurers do not require genetic data since there is no related legislation (UK[17], France, Germany, Ireland, Sweden, Finland) (E. Commission 2005: passim).

A *moratorium* applies also in Australia, New Zealand, South Africa and Canada (Lemmens 2003:57 sqq., European Commission 2005: passim).

In the US, several States have adopted statutory prohibitions and a debate is underway for a special federal law. Recently, a Bill of Law was passed in Parliament and is now pending in Congress. It is the Genetic Information Nondiscrimination Act (GINA).

This Bill of Law which represents the latest attempt at extensive regulation a) prohibits any association between the possibility of anyone to contract insurance and the amount of premium with genetic information[18], and, b) prohibits insurers from requiring insurance applicants or their relatives to undergo genetic testing[19]. It allows genetic testing for health reasons and clinical research[20], expressly dissociating these tests from

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[16] The issue is debated during the preparation of the latter, however.
[17] In the UK, in particular, there is a related provision in the Code of Ethics of the Association of British Insurers.
[18] See T. I., e.g. sec. 101, (a) (3) (d) (9) [ibid in other sec.].
[19] See T. I., e.g. sec 101, (c) (1) [ibid in other sec.].
[20] See T. I., e.g. sec 101, (c) (2) (4) [ibid in other sec.].

the question of insurance. The Bill contains definitions (for genetic data, genetic tests and genetic services)[21] and lays down sanctions[22].

C. Greek Law

The Greek law on insurance does not specifically provide for the use of genetic data in insurance[23]. Relevant here is art. 32 Act 2496/1997 under which:

"Unless otherwise agreed, health insurance includes diseases due to causes which did not previously exist or did exist but the insured justifiably ignored their existence at the time of conclusion of the insurance contract".

This article must be read together with the aforementioned provisions of the Oviedo Convention (Act 2619/1998), especially the one about the right "not –to-be-informed" and the general legal provisions on the protection of personal data (Act 2472/1997). Pursuant to the latter, the collection and processing of sensitive data (amongst which genetic data) is prohibited as a rule unless the subject has consented to it following appropriate information on the purpose of processing and on additional condition that the Authority of Data Protection has issued an authorization.

Thus, a distinction must be drawn:

- If the subject is aware of genetic data that are critical for insurance, the insurer may request such data but only under the provisos of Act 2472/1997.
- If the subject is not aware of such genetic data, the insurer may not request genetic testing because of the "not –to-be-informed" right which is safeguarded by the Oviedo Convention.

SUMMARY – CONCLUSIONS

1. There are genetic tests for a significant number of disorders with a genetic component that determine the probability of manifestation of disease with greater accuracy compared to medical testing. The degree of complexity of the evaluation of the results varies depending on individual case, and can be difficult even for experts. Therefore, the concern about the management of genetic data in life and health insurance is a legitimate one.

2. There are racial groups with greater incidence of certain genetic disorders; hence there is a risk of racial discrimination based on genetic data.

3. An extensive bioethical debate has developed with regard to access of insurance companies to the genetic data of the insured or of insurance applicants. This debate mainly revolves around two axes: a fair calculation of risk based on the principle of reciprocity, on the one hand, and protection of personality from discrimination and stigmatization on the grounds of genetic data, on the other hand.

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[21] See T. I., e.g. sec 101, (d) (6) (7) (8) [ibid in other sec.].

[22] See T. I., e.g. sec 101, (e) [ibid in other sec.].

[23] See Act 2496/1997, arts 189-225 Code of Commerce, l.d. 400/1970 (public supervision of insurance companies), p.d. 252/1996 (adaptation to relevant community law).

4. Another issue to consider is the fact that the management of genetic information with regards to access by insurance companies directly affects public support for genetic research. This has implications for the funding of research and the participation of volunteers in clinical trials, both indispensable to achieve progress in genetics. It mainly leads to avoidance of testing with injurious effects on the health of insurance applicants.

5. Greek legislation has not adopted specialised regulation for the use of genetic data in life and health insurance. Likewise no regulation exists for the operation of genetic laboratories that are the source of this information. In view of the above we recommend the adoption of special legislation according to the model followed by other countries. This legislation must strike a balance between the legitimate interests of the insurers and the insured guided by fundamental human rights.

SELECTED LITERATURE

Andrews L, Medical Genetics: A Legal Frontier (American Bar Foundation, Chicago, 1987)

Ashcroft, R. (2007) Should genetic information be disclosed to insurers? No. Bmj, 334, 1197.

Bird TD (Updated 2 October 2007). Early-Onset Familial Alzheimer Disease. In: GeneReviews at GeneTests: Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2007. Available at http://www.genetests.org. Accessed 4 October 2007.

Burke W. Genetic Testing, N Engl J Med, 2002, Vol 347, 23: 1867-1875.

European Commission, Survey on national legislation and activities in the field of genetic testing in EU Member States (L. Mathiessen-Guyader ed.), Brussels 2005 (E. Commission 2005).

Geetter, J.S. (2002) Coding for change: The power of the human genome to transform the American health insurance system. *American Journal of Law & Medicine*, **28**, 1-76.

GeneTests: Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1993-2007. Available at http://www.genetests.org. Accessed 8 October 2007.

Goldman B.R. (2005) Pharmacogenomics: Privacy in the era of personalized medicine. Northwestern journal oaf Technology and Intellectual Property, vol **4**, issue 1, 83-99.

Hall, M.A. and Rich, S.S. (2000) Laws restricting health insurers' use of genetic information: impact on genetic discrimination. *Am J Hum Genet*, **66**, 293-307.

Holm, S. (2007) Should genetic information be disclosed to insurers? Yes. *Bmj*, **334**, 1196.

HoltzmanNA, Watson MS, eds. Promoting safe and effective genetic testing in the United States: final report of the Task Force on Genetic Testing. Baltimore: Johns Hopkins University Press, 1999.

Lemmens T. (2003) Genetics and Insurance Discrimination: Comparative Legislative, Regulatory and Policy Developments and Canadian Options, Health Law Journal (special edition), 41 – 86

Low, L., King, S. and Wilkie, T. (1998) Genetic discrimination in life insurance: empirical evidence from a cross sectional survey of genetic support groups in the United Kingdom. *Bmj*, **317**, 1632-1635.

McPherson E (2006) Genetic Diagnosis and Testing in Clinical Practice, Clinical Medicine & Research, Vol 4, 2: 123-129.

Minute of the Meeting between HGC and the Single Equality Bill team, Wellington House, 2 Aug. 2007 (HGC Minute 2007)

Nationaler Ethikrat, Predictive health information in the conclusion of insurance contracts. Opinion, Berlin 2007

Pertucelli N, Daly MB, Bars Culver JO and Feldman GL (Updated 19 June 2007). BRCA1 and BRCA2 Hereditary Breast/Ovarian Cancer. In: GeneReviews at GeneTests: Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2007. Available at http://www.genetests.org. Accessed 4 October 2007.

Pfeffer, N.L., Veach, P.M. and LeRoy, B.S. (2003) An investigation of genetic counselors' discussion of genetic discrimination with cancer risk patients. *J Genet Couns*, **12**, 419-438.

Rothenberg KH and Terry SF, Before it's too late—Addressing Fear of Genetic Information, Science, 2002, Vol 297, 5579: 196-197

Warby SC, Graham RK and Hayden MR (Updated 19 June 2007). Huntington Disease. In: GeneReviews at GeneTests: Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2007. Available at http://www.genetests.org. Accessed [8 October 2007].

Kriaris-Katrani I., Genetic Technology and fundamental rights. The Constitutional protection of genetic data, Athens-Thessaloniki 1999.

ANNEX: FIGURES AND TABLES

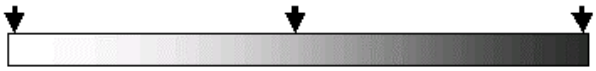

Figure 1: Schematic representation of the spectrum of genetic and environmental causes of human diseases. Adapted from GeneTests (http://www.genetests.org/)

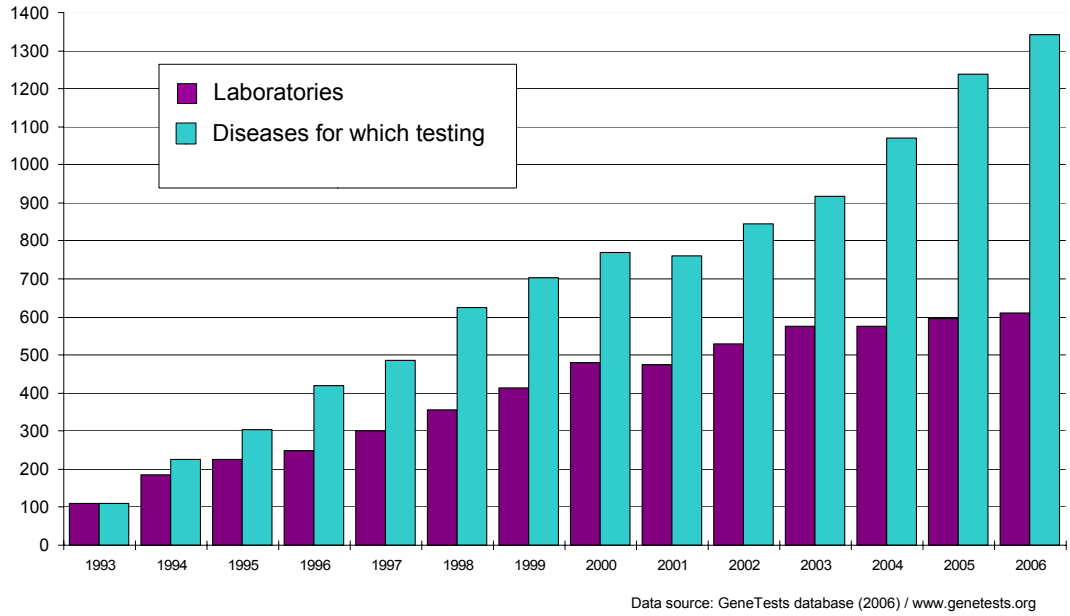

Figure 2: Evolution of the number of available genetic tests and genetic laboratories from 1993 to 2006. Source: GeneTests (http://www.genetests.org/)

Table 1: Diseases with a known genetic association per system (source: Genes and Disease, NCBI)

Blood and lymph diseases	Pendred syndrome	Epilepsy
Anaemia, sickle cell	*Cardiovascular diseases*	Essential tremor
Burkitt lymphoma	Ataxia telangiectasia	Fragile X syndrome
Gaucher disease	Atherosclerosis	Friedreich's ataxia
Haemophilia A	Long QT syndrome	Gaucher disease
Leukemia, chronic myeloid	Von Hippel-Lindau Syndrome	Huntington diseases
Niemann-Pick disease	Williams syndrome	Lesch-Nyhan syndrome
Paroxysmal nocturnal hemo-globinuria	*Diseases of the Immune system*	Maple Syrup Urine Disease
	Asthma	Menkes syndrome
Porphyria	Autoimmune polyglandular syndrome	Myotonic dystrophy
Thalassaemia		Narcolepsy
Cancers	Burkitt's Lymphoma	Neurofibromatosis
Breast and ovarian cancer	Diabetes, type 1	Niemann-Pick disease
Burkitt lymphoma	DiGeorge syndrome	Parkinson disease
Colon cancer	Familial Mediterranean Fever	Phenylketonuria
Leukemia, chronic myeloid	Immunodeficiency with Hyper-IgM	Prader-Willi syndrome
Small cell lung carcinoma	Leukemia, chronic myeloid	Refsum disease
Malignant melanoma	Severe combined immunodeficiency	Rett syndrome
Multiple endocrine neoplasia	*Male conditions*	Spinal muscular atrophy
Neurofibromatosis	Alport syndrome	Spinocerebellar ataxia
The p53 tumor-suppressor protein	Androgenic alopecia	Tangier disease
Pancreatic cancer	Prostate cancer	Tay-Sachs disease
Polycystic kidney disease	*Myoskeletal diseases*	Nodular sclerosis
Prostate cancer	Achondroplasia	Von Hippel-Lindau syndrome
Harvey Ras oncogene	Amyotrophic lateral sclerosis	Wilson's Syndrome
Retinoblastoma	Charcot-Marie-Tooth syndrome	Zellweger syndrome
Tuberus sclerosis	Cockayne Syndrome	*Nutritional and metabolic diseases*
Von Hippel-Lindau syndrome	Diastrophic dysplasia	Adrenoleukodystrophy
Digestive system	Duchenne muscular dystrophy	Diabetes, type 1
Colon cancer	Ellis-van Creveld syndrme	Gaucher disease
Crohn's disease	Fibrodysplasia ossificans progressiva	Glucose galactose malabsorption
Cystic fibrosis	Marfan syndrome	Hereditary haemochromatosis
Diabetes, type 1	Myotonic dystrophy	Lesch-Nyhan syndrome
Glucose galactose malabsorption	*Neonatal Diseases*	Maple Syrup Urine Disease
Pancreatic cancer	Achondroplasia	Menkes syndrome
Wilson's disease	Angleman syndrome	Niemann-Pick syndrome
Zellweger syndrome	Cockayne syndrome	Obesity
Ear, Nose and Throat diseases	Cystic fibrosis	Pancreatic cancer
Deafness	DiGeorge syndrome	Phenylketonuria
Neurofibromatosis	Fragile X syndrome	Prader-Willi syndrome
Pendred syndrome	Marfan Syndrome	Porphyria
Diseases of the Eye	Prader-Willi syndrome	Refsum disease
Best disease	Severe combined immunodeficiency	Tangier disease
Glaucoma	Waardenburg syndrome	Wilson's disease
Gyrate atrophy of the choroid and retina	Werner's syndrome	Zellweger disease
	Williams syndrome	*Respiratory diseases*
Retinoblastoma	Zellweger syndrome	α-1-antithrypsine deficiency
Female-Specific Diseases	*Nervous system diseases*	Asthma
Breast and ovarian cancer	Adrenoleukodystrophy	Cystic fibrosis
Rett syndrome	Alzheimer disease	Small cell lung carcinoma
Gland and hormone diseases	Amyotrophic lateral sclerosis	*Skin and connective tissue diseases*
Adrenal hyperplasia, congenital	Angelman syndrome	Androgenic alopecia
Adrenoleukodystrophy	Ataxia telangiectasia	Diastrophic dysplasia
Autoimmune polyglandular syndrome	Cockayne syndrome	Ellis-van Creveld syndrome
	Charcot-Marie-Tooth syndrome	Marfan syndrome
Breast and ovarian cancer	Deafness	Malignant melanoma
Cockayne syndrome	Duchenne muscular dystrophy	Menkes syndrome
Diabetes, type 1		Porphyria
Diastrophic dysplasia		
Multiple endocrine neoplasia		

Table 2 : Examples of genetic diseases for which a genetic predisposition test exists

Disease	Gene/s, genetic region	Power of detection	Incidence in the general population	Penetrance	Age at onset	Cost* (euros)
Huntington's Disease	HD (IT 15), 4p16.3	100%	3-7/100.000 (varies depending on ethnic origin)	36-39 repeats: strong probability, >40 repeats: 100%	35-44	165
Early-Onset Alzheimer (EOFAD)	PSEN1, 14q24.3 PSEN2, 1q31-q42 APP 21q21	5-70% depending on the method	41,2/100.000	AD3 (PSEN1): 100%, AD4 (PSEN2): 95%	40-59	490-4400
Hereditary Breast/ Ovarian Cancer	BRCA1, 17q21 BRCA2, 13q12.3	>88% in families with confirmed association with BRCA1/2	1/500-1/1000 carries a genomic mutation (>1% in Ashkenazi Jews)	3.2-85% Significant differences depending on age, type of mutation, type of cancer and model of calculation	30-70	390-1900
Thrombosis Risk Factor (Leiden V factor)	F5, 1q23	100%	10-15% heterozygotes in Greece (1/5000 homozygotes)	0,19%-0,45% per year – 0,10% for non-carriers of the mutation	The disease may be manifested also after 60	55
Muscular dystrophies (e.g. Duchenne, Becker)	DMD Xp21.2	6-85% depending on the method	1/5000 births of male infants	100% in males, varies in females (8% cardiomyopathy)	Symptoms from the age of 2, immobility in adolescence. Dilative cardiomyopathy after 40 in female heterozygotes	410
Haemochromatosis	HFE, 6p21.3	60-90%	1/200-1/400 homozygotes, 11% carriers of the gene	Depending on genotype: from 0,5% to nearly 100%	40-60 (males), after menopause (females)	80-1100
Autosomal Dominant Polycystic Kidney Disease	PKHD1, 6p21.1-p12	2-75%	1/20000-2/40000	100%	From birth or childhood	775-7700
Familial Mediterra-nean Fever	MEFV, 16p13	70-90%	1/3-1/7 carriers (they do not manifest the disease)	Unknown, probably underdiagnosed	2-25 usually	290-440
Amyotrophic Lateral Sclerosis	Many and varying	3-20%	4-8/100.000 (90% without family history)	Unknown	40-60	400

*From the network diagnogene (www.diagnogene.com). The cost varies depending on the number of tested mutations.