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Council of Europe – Committee on Bioethics

Genetic Testing for Health Purposes in Central and Eastern Europe

Edited by J. Glasa, H. Glasová

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Regional International Bioethics Conference on Genetic Testing for Health Purposes in Central and Eastern Europe

29-30 May 2014

Bratislava, Slovak Republic

Proceedings

Genetic Testing for Health Purposes in Central and Eastern Europe

Proceedings of the Council of Europe Regional International Conference
„Genetic Testing for Health Purposes in Central and Eastern Europe“
May 29 – 30, 2014, Bratislava, Slovak Republic

Edited by J. Glasa, H. Glasová

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FOREWORD

It is our pleasure and a great honour to introduce to you this volume containing the Proceedings of the *Regional International Bioethics Conference – Genetic Tests for Health Purposes in Central and Eastern Europe*, which took place in Bratislava on May 29 – 30, 2014, as an activity sponsored by the Committee on Bioethics (DH-BIO) and its Secretariat within the program DEBRA.

The truly unique features of the conference were at least two-fold: 1. the main topic chosen was dealing with the rapidly, exponentially growing area of contemporary medicine and health care – medical genetics in general, and with one of its most powerful working arms – genetic tests in particular, all this being dealt with from a specific viewpoints of international bioethics and bio-law; 2. the participants – invited delegates to the conference, were stemming from the countries of Central and Eastern Europe that have shared multifaceted, complex, and rather similar experiences of the relatively recent past, and, more importantly, also more or less similar present date and emerging challenges, when aligning their medical practices and health care systems to face and deal with their inherent advances and shortcomings in their continuous efforts to implement and develop medical genetics as an integral part of those. All this to provide also the necessary respect and protection of human dignity and rights for their citizens, especially the patients and their relatives, while implementing eagerly and wisely these new powerful technologies and sciences for the individual and common good, i.e. for the purposes of protection, and also for development of a good health, and, hopefully, of a good life.

The conference participants greatly benefited from the state-of-the-art inputs provided by the distinguished invited speakers, and also from their own, brought in, concrete inputs, concerning the varying situations in their respective countries that they were able to share and discuss with their colleagues from, sometimes, very interesting and useful new angles. The space and attention that were put to this exchange and common discussion part of the meeting did proved itself being both very interesting and useful. And also encouraging. Especially, when facing the long lasting, country-specific situations, where the legal, or educational-informational progress is very difficult to achieve, even with much extraordinary effort and additional expert work, let aside lagging behind (in comparison with some other parts of Europe) in respective technological, organizational and health policy realms.

It is our duty and honour to thank cordially to all contributors to this volume, who were kind enough to provide their original manuscripts, as well as to the delegations that were able to share the information and insight for the better as seen from their countries' perspectives.

We would also like to thank the Secretariat of DH-BIO for an excellent help and support both in organizing the meetings itself, but also in putting together this publication.

We hope, dear readers, that you find the following pages interesting and useful.

Jozef Glasa & Helena Glasová, volume editors

Bratislava, October 2014

OPENING ADDRESS

Laurence LWOFF

Bioethics Unit, Council of Europe, Strasbourg, France

Dear members of the Honorary Presidium
of the Conference,

Honorable members of the countries' delegations,

Distinguished conference speakers and chairs,

Ladies and gentlemen,

It is both an honor and a pleasure to be here today, in Bratislava, as the Representative of the Council of Europe, at the opening of this Conference. And this in many respects.

This year we are celebrating the 15th anniversary of the entry into force of the *Convention on Human Rights and Biomedicine* (Oviedo Convention). Slovakia was one of the first countries to ratify the Convention enabling it to enter into force.

The very first regional bioethics conference sponsored by the Council of Europe took place in Bratislava already in January 1992. Since then Slovakia has greatly contributed to raising awareness on and to facilitating implementation of the Convention by hosting, with this event, already six international conferences, the first one in 1999, focusing on the Convention and its additional protocols, including, in 2002, a conference on ethics of human genetics.

Genetic testing will be at the center of this conference organized under the auspices of Mrs. Zuzana Zvolenská, minister of health, represented here by Dr. Ján Rosocha, whom I wish to thank particularly. But also this conference is held with the support of the Slovak Medical Association, the Slovak Medical University in Bratislava, and of the Institute of Medical Ethics and Bioethics n.f.

I wish to thank all of them for their involvement in the organization of this conference, together with the Bioethics Unit of the Council of Europe in the framework of its cooperation activities (Program DEBRA).

Genetics is clearly the field, which has seen very important developments, in particular in the last 15 years. A lot of benefits for human health are expected from these positive achievements of science and technology. Research in this field is the source of a great hope for better understanding of etiology of so many diseases and development of appropriate treatment and prevention means. Even though the situation in European countries may vary, medical genetics and genetic testing are becoming more and more an integral part of the health care. The applications of genetics expand also much outside the medical field.

But medical genetics and genetic testing provides for greater possibility to enter into the biological intimacy of all human beings, raising concerns about privacy and possible discrimination on the basis of an individual's genetic characteristics.

All these issues needed to be addressed to ensure proper protection of human rights enabling thereby to promote proper use of this important tool for the benefit of human health.

This was the main objective of the *Additional Protocol to the Convention on Human Rights and Biomedicine on Genetic Tests for Health Purposes* elaborated by the Council of Europe and opened for signature in 2008. This Protocol complements the Oviedo Convention, developing further this legal corpus, which has now gain a reference status at the European, but also at the global level.

This Protocol, for the drafting of which the Committee on Bioethics of the Council of Europe benefited a lot from the work already done by several professional associations and some international organizations, in particular the European Society of Human Genetics, was unanimously adopted by the Committee of Ministers and thus opened for signature and ratification. It already had influenced several national legislations that were in development during and after the Protocol's adoption.

This conference will provide an opportunity to examine developments in genetic testing and the human rights challenges they have raised. An opportunity, also to better understand the possible difficulties encountered, in particular in the Central and Eastern Europe, in dealing with those challenges, which are addressed in the Additional Protocol.

Taking into account these problems, it is particularly important for the development of legislation and good practices that are respectful of the fundamental values, on which the provisions of the Protocol are based. I trust that this symposium will contribute to the achievement of that objective and I wish to thank in advance the speakers, who have agreed to share their knowledge, as well as the participants for their input and contribution in the discussion that will take place during these two days.

Thank you for your attention!

Correspondence to: Mrs. Dr. Laurence Lwoff, Head, Bioethics Unit, Human Rights Policy and Development Department, Human Rights Directorate, Directorate General I, Council of Europe, F-67075 Strasbourg Cedex, France,
e-mail: laurence.lwoff@coe.int

Article 1 – Object and purpose

Parties to this Protocol shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the tests to which this Protocol applies in accordance with Article 2.

Article 2 – Scope

1 This Protocol applies to tests, which are carried out for health purposes, involving analysis of biological samples of human origin and aiming specifically to identify the genetic characteristics of a person which are inherited or acquired during early prenatal development (hereinafter referred to as "genetic tests").

2 This Protocol does not apply:

a) to genetic tests carried out on the human embryo or foetus;

b) to genetic tests carried out for research purposes.

3 For the purposes of paragraph 1:

a) "analysis" refers to:
- *i. chromosomal analysis,*
- *ii. DNA or RNA analysis,*
- *iii. analysis of any other element enabling information to be obtained which is equivalent to that obtained with the methods referred to in sub-paragraphs a.i. and a.ii.;*

b) "biological samples" refers to:
- *i. biological materials removed for the purpose of the test concerned,*
- *ii. biological materials previously removed for another purpose.*

Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes (2008)

GENETIC TESTS – OVERVIEW OF THE SITUATION IN THE LIGHT OF THE TECHNOLOGICAL DEVELOPMENTS: AN EXAMPLE OF THE CZECH REPUBLIC

Milan Macek

Department of Biology and Medical Genetics, Charles University Prague, 2nd Faculty of Medicine and University Hospital in Motol, Prague, Czech Republic

Extended Abstract

The main aim of the presentation was to provide an overview on the increasing disparities in terms of the rapid production of biomedical data, by e.g. next generation sequencing technologies (NGS) in genetics/genomics, and lagging clinical validity and utility of such data within the domain of health care. The falling price of DNA sequencing which now exceeds Moore's law for semiconductors and the relative rapid increase in genetic testing outside of the traditional "germ line" genome domain i.e. testing of somatic mutations in oncology, minimal residual disease in hematooncology, microbiology, creates strong pressures on finite resources in all solidarity principle based European health care systems. Moreover, some low-resourced countries are in the risk that they will be completely left out of the "omics" biomedical revolution and are increasingly lagging behind with relevant health care applications.

In the absence of regulation every medical device (e.g. sequencer) will "find its patient" and rapid commercialisation of diagnostic services compounds the situation by increasingly applied "profit-oriented" testing and unwillingness to share data financed from public health care funds. A recent study carried out in Germany found out that up to 70% of medical indications for genetic testing were not substantiated by evidence based approaches, while in most other countries the situation remains unmapped.

Very often genetic testing is used as a last resort when standard differential diagnostic processes had been exhausted. This "ex vacuo" approach in very rare diseases runs the risk that even at high sensitivity and specificity of the test applied its outcomes could be biased by random mistakes appearing at a higher rate than the prevalence of the disorder under examination. Very good examples of incidental findings come from other fields, such as radiology (e.g. from MRI scans), where duties "to care and do no harm" in medicine may lead to increase in subsequent diagnostic procedures and thus also in costs.

Another important concern is the fact that European clinical genetic services are understaffed (clinicians, genetic counsellors, nurses), and there are marked disparities between various countries. The European Society of Human Genetics (www.eshg.org) is monitoring genetic services provision in Europe on its website.

The Czech Republic could be used as an example for the remainder of Central and Eastern Europe. On the positive side medical and laboratory genetics are well recognised professional specialities, with board exams, medical societies and a thriving state and private sectors, mostly operating according to European guidelines and recommendations. Law No. 96/2001Coll. codified the Oviedo convention within the Czech legal system. Law No. 373/2011 Coll. is specific for genetic testing and has adopted most of the provisions of the Additional protocol on genetic testing for health care purposes of the Council of Europe, except for clinical utility clause, which was dropped at the last minute by the Parliament during examinations of the draft proposal prepared by the Czech Society of Me-

dical Genetics. Examples of misuse of genetic testing and the lack of legal support for revision processes carried out in response by the Czech health insurance companies were given. The aforementioned professional association published in 2007 an open editorial in the most of country's medical journals warning against the "misuse of genetic testing and potential for discrediting of the entire profession". Based on well publicised cases of misuse of genetic testing, where suspicions even ran very high within the political class (investigation is still ongoing), the Czech Ministry of Health started the work on necessary revisions of the Law No. 373/2011Coll. §28-29 in Spring 2014 in order to render legal safeguards for responsible and evidence-based provision of the modern genomic technologies within the national health care. Distinction has been made between trans-generational and intra-generational aspects of medical genetic services, their various roles, and associated necessity for specific legal provisions for patients and their families.

M.M. was supported by the Czech Ministry of Health: 00064203 –IP6003, CZ.2.16/3.1.00/24022, RD-connect.eu (FP7-305444) and Norway Grants (NF-CZ11-PDP-3-003-2014).

Correspondence to: Prof. Milan Macek, MD, D.Sc., Department of Biology and Medical Genetics, 2nd Faculty of Medicine and University Hospital in Motol, V Úvalu 84, CZ-150 06 Prague 5, Czech Republic,
e-mail: milan.macek.jr@ lfmotol.cuni.cz

Article 3 – Primacy of the human being

The interests and welfare of the human being concerned by genetic tests covered by this Protocol shall prevail over the sole interest of society or science.

Article 4 – Non-discrimination and non-stigmatisation

1 Any form of discrimination against a person, either as an individual or as a member of a group on grounds of his or her genetic heritage is prohibited.
2 Appropriate measures shall be taken in order to prevent stigmatisation of persons or groups in relation to genetic characteristics.

Article 5 – Quality of genetic services

Parties shall take the necessary measures to ensure that genetic services are of appropriate quality. In particular, they shall see to it that:

a) genetic tests meet generally accepted criteria of scientific validity and clinical validity;

b) quality assurance programme is implemented in each laboratory and that laboratories are subject to regular monitoring;

c) persons providing genetic services have appropriate qualifications to enable them to perform their role in accordance with professional obligations and standards.

Article 6 – Clinical utility

Clinical utility of a genetic test shall be an essential criterion for deciding to offer this test to a person or a group of persons.

Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes (2008)

MEDICAL GENETICS AND HEALTH CARE SERVICES

Borut Peterlin

Clinical Institute of Medical Genetics, University Medical Center Ljubljana, Ljubljana, Slovenia

Introduction

The Health for Growth Program, the third multi-annual program of the European Union in the field of health (period 2014-2020) focuses, among other issues, on the development of innovative and sustainable health care systems, prevention of diseases, and on increasing the access to health care (1).

All mentioned areas are very relevant to the field of genetic services provision. The aim of genetic services is to respond to the needs of individuals and families who are threatened by a genetic disease. In particular, to their wish to know whether they are at risk of developing or transmitting a genetic disease (2). Rare diseases affect between 27 and 36 million Europeans and it is estimated that about 80% of rare diseases could be attributed to the genetic etiology. Rare diseases are characterized by several challenges: the diagnostic process is often complex, time-consuming and painful to the patient; the genetic information might not always be sufficiently and clearly communicated to the patients and their families. Health systems should therefore improve the access to genetic services, implement systems for quality assurance, and translate wisely new technologies into daily clinical practice.

Access to genetic services

Access to genetic services depends on several factors, including the capacity of medical professionals to recognize a potential genetic etiology and to refer patients to genetic services, as well as on capabilities and capacities of the genetic services to provide adequate service.

There is sufficient evidence to say that medical specialists, including general practitioners, gynecologists, and pediatricians feel the need to improve their competencies in genetic medicine. Medical genetics education focused upon different medical professionals target groups could contribute in an important manner to the improvement of referrals of patients and family members for genetic counseling and testing (3).

On the other hand, according to the *Orphanet* (4), 82% of EU member countries cover genetic testing of less than 500 diseases out of more than 3000 that have been associated with human diseases so far (5). This implies that genetic diagnosis in the majority of EU member countries, especially the smaller ones, importantly depend on the cross-border access to the genetic services. In several of them, more so in the Eastern and Southern European countries, the national health care systems have not established pathways to comprehensive genetic diagnostics in spite of the favorable EU policy background – *Directive on the application of patient's rights in cross-border healthcare* (6).

Both the improvement of education and competencies of the medical professionals and of the capabilities of the genetic services, do present important opportunities to assure the appropriate access to genetic medical services.

Quality of genetic services

Accreditation and certification of genetic services are important means to ensure and control their quality. International quality standards on the technical competence

of medical laboratories (ISO15189) have been issued, and the schemes for external quality assessment (EQA) in genetic testing have been developed. Nevertheless, according to *Orphanet/EuroGenetest* database, only 11% of EU laboratories providing genetic tests are effectively accredited, and only 33% participated in at least one EQA scheme in 2011 (7). Genetic services quality committee at the European Society of Human Genetics is currently launching a new pilot project focused on the quality assessment of genetic counseling services.

Introduction of clinical genomics into the health service

New genetic technologies, especially Next Generation Sequencing (NGS) applications and array-based technologies are being increasingly used in the clinical diagnostics. While introduction of new technologies into the clinical laboratories presents a significant cost in terms of equipment and personnel, as well as additional clinical applications, new diagnostic approaches significantly increase sensitivity of genetic testing. Classical genetic testing for several disorders comprised of testing several genes (in succession), which resulted in a high price of genetic testing; NGS applications enable testing for tenths of genes or even all genes in the genome (exome) in one test and has the potential to significantly improve the yield and reduce the cost of genetic testing. Exome/genome sequencing applications also provide means to test potentially any of the known gene – disease associations, which significantly increases the number of diseases that can be tested in the single laboratory.

There are, however, still several challenges in terms of clinical implementation of NGS applications: there is lack of standardization (8) and clinical guidelines, of the best practices in terms of informed consent procedures and incidental findings management (those are being developed at present). And there is as yet also somewhat insufficient availability of the necessary equipment and expertise in some regions/countries/health care facilities.

Development of future genetic services

Future organization of genetic services needs to cope with increased demand thereof, both in terms of genetic testing and genetic counseling, and of an effective translation of new genome technologies into the clinical practice. Multidisciplinary collaboration among geneticists and other medical specialists needs to be further developed, and an integration of medical genetics into primary care is expected. Reconfiguration of professional roles both for geneticists and for other medical specialists will be needed for an adequate provision of future genomic medicine. In this process, several barriers will need to be overcome, including existing professional boundaries, inadequate professional development schemes, and a lack of necessary preparedness of the health care system.

To assure sustainability of health care systems, a thoughtful prioritization of genetic testing will be necessary. Prioritization might be based on the usefulness of a test with regard to the patient care, including treatment options, potential to improve quality of life and to extend life expectancy, as well as on social factors.

There is also a clear need for adoption of sound and effective health policies, legislative and other measures that are necessary for developing of a coherent and comprehensive national frameworks for genetic services, as suggested in the Council of Europe recommendation on the impact of genetics on the organization of health care services and on training of the health care professionals (9).

Conclusions

Existing challenges in terms of access to genetic services of an appropriate quality, as well as of successful translation of the more efficient, novel genomic technologies into the mainstream medicine do require an adequate concerted action of several key stakeholders; sound and widely accepted international professional and policy recommendations might considerably facilitate the process.

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Abstract*

The paper gives an overview of the most important practical challenges of the implementation of genetic services within the contemporary health care systems in Europe. The increasing availability of modern high throughput laboratory technologies operating at progressively decreasing costs per a parameter measurement provides for a considerable increase of genetic data and knowledge. Available genetic services are in many places not fully able to meet these novel opportunities and growing demands. New approaches need to be sought and implemented within the resources stricken health care systems to enable a successful and sustainable implementation of genetic/genomic medicine in contemporary and future health care to meet properly the patients health needs in effective diagnostics, treatment, and prevention.

Key words: genetic medicine, health care, sustainability, efficacy, public health

Abstrakt*

Práca poskytuje prehľad najdôležitejších praktických problémov spojených s implementáciou genetických služieb v rámci súčasných zdravotníckych systémov v Európe. Narastajúca dostupnosť moderných vysoko efektívnych laboratórnych technológií za súčasne sa znižujúcej ceny jednotlivého stanovenia zapríčiňuje značný nárast genetických údajov a poznatkov. Súčasné genetické služby v niektorých prípadoch nie sú schopné v plnej miere udržať krok s týmito novými možnosťami a narastajúcimi požiadavkami. Je potrebné hľadať a uplatňovať nové prístupy, ktoré umožnia vo finančne obmedzených podmienkach zdravotníckych systémov úspešnú a udržateľnú implementáciu genetickej/genomickej medicíny v súčasnej a v budúcej zdravotnej starostlivosti, aby sa naplnili potreby pacientov v oblasti efektívnej diagnostiky, liečby a prevencie.

Kľúčové slová: lekárska genetika, zdravotná starostlivosť, udržateľnosť, efektívnosť, verejné zdravie

*Abstracts by the editors./Abstrakty spracovali zostavovatelia.

Correspondance to: Prof. Borut Peterlin, Clinical Institute of Medical Genetics, University Medical Center Ljubljana, Šlajmerjeva 3, Ljubljana, Slovenia, e-mail: borut.peterlin@guest.arnes.si

GENETIC TESTS VIA THE INTERNET
Limitations and Risks

Pascal Borry

Centre for Biomedical Ethics and Law,
Department of Public Health and Primary Care,
University of Leuven, Leuven, Belgium

Introduction

Since 2007 various commercial companies have started to advertise and sell genetic tests directly to consumers. (1) Based on notions of autonomy, empowerment, prevention, convenience, and privacy, those companies have usually emphasized that individuals should have a more active role in the access to genetic tests and in the storage and protection of their genetic information. Moreover companies have underlined the empowering side, as this would provide provides "the foundation for truly personalized medicine in which individuals are empowered not only with self-knowledge of their genetic risk, but also with the ability to take informed actions to prevent disease and preserve health"(2).

Direct-to-consumer (DTC) genetic testing encompasses different situations. Firstly, it refers to a situation of "advertising of such tests directly to the public, with the actual ordering of the investigation and receipt of results involving a health care provider". Secondly, it refers to the situation "where, in addition to advertising to the public, the request for testing is initiated by the patient and results are, in turn, provided directly to the patient, independently of the person's usual medical practitioner." (3) Also the report of the Human Genetics Commission included in their analysis situations where "tests are commissioned by the consumer but where a medical practitioner or health professional is involved in the provision of the service." (4) This inclusion is important as not all concerns with regard to DTC genetic testing are removed if a medical practitioner is involved somewhere in the process of ordering a genetic test. (5)

The current offer of DTC genetic tests is broad, and includes both health-related and non-health-related tests. At the level of health-related tests various companies offer susceptibility tests for common complex disorders, carrier tests for autosomal recessive disorders, pharmacogenomic tests, and so-called 'lifestyle' tests. Non-health-related tests include testing for traits, such as athletic performance, ancestry and genealogical tests, as well as paternity tests. Over the years the number of disorders and traits analysis has often been increasing. Moreover, at the technical level instead of analysing single nucleotide polymorphisms resulting from genotyping, companies are currently starting to offer whole genome or exome sequencing.

This paper aims to provide an overview of (a) the concerns related to DTC genetic testing and (b) the regulatory approaches that have been presented and/or implemented.

Limitations and risks

The offer of DTC genetic tests has led to various concerns. Especially, various professional societies (6-10), National Bioethics Committees (11-14) or national advisory committees (4;15) addressed recently the topic. At the European level, the European Academies of Science and the Federation of European Academies of Medicine have also published a report on this issue. (16) In this article following concerns will be highlighted: 1) Limited clinical validity and utility; 2) Potential negative psychological impact; 3) Absence of pre- and post-test counseling and an adequate informed consent procedure; 4) Absence of individualized medical supervision; 5) Potential burden on the healthcare system.

Limited clinical validity and utility

When assessing the quality of genetic tests, the ACCE model has been proposed as a useful tool. (17;18) This tool integrates a set of 44 questions that related to the analytical validity (i.e. how accurately and reliably can the test measure the genotype of interest?), clinical validity (i.e. how consistently and accurately is the test able to detect or predict the intermediate or final outcomes of interest?), clinical utility (i.e. how likely is the test is to significantly improve patient outcomes?), and the ethical, legal and social issues refer to the ethical, legal, and social implications that may arise in the context of using the test.

In view of these criteria, many commentators have criticized the limited clinical utility and validity of DTC genetic tests. (19-23). As for example, Janssens et al. (24) with regard to the provision of risk profiles for common complex disorders advanced that "there is insufficient evidence to conclude that genomic profiles are useful in measuring genetic risk for common diseases or in developing personalized diet and lifestyle recommendations for disease prevention." Common complex disorders develop due to a complex interaction of multiple genes and environmental factors. Each genetic and environmental factor often contribute only a modest fraction of the risk of developing the disorder, therefore, making it extremely difficult to assign an accurate and meaningful degree of risk to each different factor. In the same line, the Government Accountability Office concluded that the tests they analyzed "mislead the consumer by making health-related predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers." (25)

On November 22, 2013 the US Food and Drug Administration (FDA) ordered the US-based company 23andme to stop marketing its "Personal Genome Service" (PGS), a health-related direct-to-consumer (DTC) genetic testing service (26). In their warning letter, the FDA showed especially concerns about the health claims that were made by this company: "Some of the uses for which PGS is intended are particularly concerning, such as assessments for BRCA-related genetic risk and drug responses (e.g., warfarin sensitivity, clopidogrel response, and 5-fluorouracil toxicity) because of the potential health consequences that could result from false positive or false negative assessments for high-risk indications such as these. For instance, if the BRCA-related risk assessment for breast or ovarian cancer reports a false positive, it could lead a patient to undergo prophylactic surgery, chemoprevention, intensive screening, or other morbidity-inducing actions, while a false negative could result in a failure to recognize an actual risk that may exist. Assessments for drug responses carry the risks that patients relying on such tests may begin to self-manage their treatments through dose changes or even abandon certain therapies depending on the outcome of the assessment. For example, false genotype results for your warfarin drug response test could have significant unreasonable risk of illness, injury, or death to the patient due to thrombosis or bleeding events that occur from treatment with a drug at a dose that does not provide the appropriately calibrated anticoagulant effect. These risks are typically mitigated by International Normalized Ratio (INR) management under a physician's care. The risk of serious injury or death is known to be high when patients are either non-compli-

ant or not properly dosed; combined with the risk that a direct-to-consumer test result may be used by a patient to self-manage, serious concerns are raised if test results are not adequately understood by patients or if incorrect test results are reported."

Potential negative psychological impact

Concerns were raised that consumers might misinterpret genetic test results or might experience psychological distress caused by abnormal test results. Consumers who obtain a test result that reveals an increased risk for a certain condition may over-estimate the risk they have of developing disease and this may cause undue stress and anxiety and unnecessary follow-up tests or treatments. In contrast, consumers with results that suggest standard or inferior than average risk of developing a disorder may understand this as meaning that they no longer have to worry about leading a healthy life style. (27;28)

Some studies have analyzed the psychological impact of consumers receiving risk profiles for common complex disorders. Bloss et al. reported that in a selected sample of subjects who completed follow-up after undergoing consumer genomewide testing, such testing did not result in any measurable short-term changes in psychological health, diet or exercise behavior, or use of screening tests. As the study was peformed within a self-selected group, the authors didn't make any claims about the potential effect of this type of genetic testing on the population at large. (29) In a more recent study, Bloss et al. reported about the long term psychological, behavioural and clinical impacts of genomic risk testing for common diseases. The researchers concluded that genomic testing was not associated with long term psychological risks. (30)

These studies indicate that concerns about a negative psychological impact of DTC genetic testing on individuals who obtained such testing might be exaggerated. Nevertheless, as the mentioned studies were limited due to a self-selected group and the focus on genomic risk testing for common diseases, it might not be representative for the whole population, neither for other types of tests, such as targeted, exome or whole genome sequencing.

Absence of pre- and post-test counseling and of an adequate informed consent

In a review of policy guidelines and position papers on DTC genetic testing, Skirton et al. showed that "all documents in the review considered the potential for harm due to lack of understanding or information about the test, and particular recommendations focussed on information that should be available to consumers." (31) In particular, Skirton et al reported the importance of various types of information (and related issues) when offering a test: the purpose and nature of the test, the risks associated with testing, accurate information on clinical utility, the scientific evidence supporting the use of the test (including validity), the availability of counselling by a health professional, the availability of treatment or lack of treatment for the condition, the format and presentation of the results, the implications of the results, the quality regulation of the laboratory, the management and care of the sample, the confidentiality of results and security of samples, the subsequent use or storage of samples, sources of independent information, possible impact on insurance or employment.

The fact that many companies only have written information on their website and don't allow for pre-test face to face information has been a matter of concern. Moreover, questions were raised whether about the commercial nature of the information and potential overstatements of the utility of the tests. In its statement, the European Society of Human Genetics wrote the following: "Research on DTC advertising of prescription medicine has shown that this has created an inappropriate demand for medications. Moreover, it has shown that various advertisements for drugs have been misleading. Overstatement of effectiveness or minimization of risk has led to inadequate or inappropriate changes in medication, diet or lifestyle by consumers. DTC advertising of genetic tests for health-related purposes runs the same risks as DTC advertising of prescription medicine in this regard. Aggressive marketing strategies and slogans for DTC genetic testing might overstate the potential for predictive information of such tests and overrate its future health implications. All this is likely done to increase test uptake and artificially create new demands, that is, to earn money. We strongly believe that every advertisement should conform to the same international standards and guidelines that apply for advertisement of drugs and medical devices. Among other issues, the advertisement should be accurate and not misleading, claims should be transparent and supported by current evidence, and complete and accurate information about the test limitations, risks and benefits should be provided."(6)

With regard to genetic counselling, various commentators have criticized the lack of involvement in DTC genetic testing of an appropriately trained person to help the individual or the family to understand the medical facts of the disorder and the options on how to deal with it. In the cases that genetic counselors were involved, critiques were rather focused on the potential conflict of interest that may arise when the healthcare professionals involved in the counseling are employed by or linked to the companies selling the tests. In this case impartial health advice might be compromised. Concerns were also raised with regard to the reduction of the informed consent process to signing a test order or clicking a box. (6) Moreover, since biological samples are taking in the privacy of someone's home, there is no way of controlling for the identity of the sample provider. Testing of third parties without adequate consent becomes possible and rather impossible to control.

Absence of individualized medical supervision

In a review of policy guidelines and position papers on DTC genetic testing, Skirton et al. showed that "strong recommendations were made about the need to involve trained and quali_ed health professionals to provide both accurate information and pre- and post-test counselling." This is a particular concern as many DTC genetic testing companies operate without the supervision of a qualified health professional. Whether or not this should be a physician is not specified in every document. (31) The European Society of Human Genetics mentioned that the "offer of genetic tests providing health-related information, in the absence of clinical indications and individualized medical supervision, may compromise patient health. Key concerns are the provision of sufficient information about the purpose and appropriateness of testing, its possibilities and limitations, as well as the clinical significance of testing. An involvement of independent medical professionals could avoid the waste of money on tests that are clinically irrelevant. In addition, the cost and adverse psychosocial effects of unnecessary follow-up or medical investigations could be avoided." (6) The mere involvement of a physician in this process might not resolve all the concerns with regard to DTC genetic testing, as concerns with regard to the clinical validity or clinical utility of tests might remain.

Potential burden on the healthcare system

Although the actual impact of DTC genetic testing on public healthcare systems remains largely understudied, several studies have indicated that consumers would contact or have contacted healthcare professionals. A British study reported that 78% of the study participants would consult a healthcare professional on their test result. (32) Another study found that 86.9% of the general public would seek more information about test results from their doctor. (33) The degree to which these stated intentions translate into actual physician visits is unclear. Another study showed that 53% of those who had used a test had visited their physicians regarding the results and 10% planned to do it. (34) As commented earlier "for health systems striving to contain costs, even a small influx in use is a potential health policy issue, particularly given the questionable clinical utility of the tests offered by DTC companies." (35)

Other concerns

Other concerns with regard to the activities of DTC companies include the research activities of these companies performed on submitted samples and information without adequate informed consent or monitoring by a research ethics committee (36). In addition, concerns were raised about what is happening to the samples and data when a company is going bankrupt (37). Moreover, when looking at the policies of DTC genetic testing companies, it is clear that various companies are testing minors which is in opposition to clinical guidelines. (38; 39)

Policy strategies

In the following part of the article we will discuss some policy strategies that have been implemented or suggested, and that might impact DTC genetic testing services. In particular, we will focus here on 1) education for the general public and health care professionals, 2) initiatives for self-regulation, 3) the call for implementing information and advertising standards, 4) the provision of genetic tests through medical doctors, 5) the penalization of users, or 6) the sanctioning of non-consensual testing. We will not expand on this in this article, but it is worth mentioning that some proposals were also made to have quality labels for DTC genetic testing. In the Netherlands, a permit system exists that has an impact on the provision of DTC genetic testing. (40)

Education for the general public and health care professionals

Various policy documents have mentioned the need to inform the general public and health care professionals about the limitations of DTC genetic testing. (31) A report of the Belgian Superior Health Council for example emphasized the importance of information provision: "In light of growing number of companies selling and advertising genetic tests DTC, the Superior Health Council considers that it is crucial that information is available for healthcare professionals and the general public that gives background on genetic testing and describes the provision of genetic testing services. On one hand, it is important to underline that clinically validated and medically appropriate genetic tests are offered in clinical services for those that need them and that these are reimbursed by the healthcare system. On the other hand, it is important that information is available about the limitations and concerns of the tests that are currently advertised, provided or sold through the internet."

Also the Nuffield Council of Bioethics recommended "that appropriate publicly-funded health service websites should include general information for the public about direct-to-consumer genetic profiling services provided by commercial companies. This information should include reference to: potential risks and benefits; any difficulties with establishing clinical validity; the possibility of finding out about conditions for which treatment is not available; the special case of children; and whether it could be necessary for consumers to inform life, mortgage or travel insurance companies of the results of any tests, either at the time or in the future. We further recommend that governments should require details about where to find this information to be included in the advertising and information provided by companies selling genetic profiling services in their countries." (41)

Over the past years, various leaflets providing information on DTC genetic tests were developed. (42;43) A decision support tool for health professionals was also developed. (44)

Encouraging industry self-regulation

The Human Genetics Commission of the UK took important initiatives in order to set standards and principles with regard to DTC genetic testing and to promote their consistent use at an international level. In a document (4), it developed a common framework of principles for DTC genetic testing services with attention to standards with regard to marketing and advertising, information for prospective consumers, counselling and support, consent, data protection, handling of the samples, laboratory processes, interpretation of the results, provision of the results and procedures to tackle complaints. In its principle 1.1., the Human Genetics Commission made clear that the goal of those principles were to ensure "good practice" and to safeguard the interests of the consumer. Although praised for its intention, this common framework was also criticized. In a public reaction during the consultation phase of the document of the Human Genetis Commission, the Professional and Public Policy Committee of the European Society of Human Genetics, for example, stated that the "guiding principles focus too much on the requirements the test providers should fulfill while paying too little attention to the quality of the genetic tests that are being sold. The PPPC remains concerned about the quality of the tests provided and believes that the clinical validity (and not only the analytical validity) of genetic tests should be proven before one can even begin to consider selling such tests directly-to-consumers." (45) Moreover, the PPPC advanced that the Principles reduced "reduce the informed consent process to a process in which the test providers have to provide sufficient and appropriate information" and that "the current Principles do not put enough responsibility on the test providers to ensure that the consumers comprehend the disclosed information, act voluntarily, and are competent to act and consents to all elements of the consent form. Providing information does not substitute obtaining informed consent." (45) Although the common framework was developed in dialogue with representatives of the DTC genetic testing industry, the impact of the common framework on this industry remained limited.

Implementation of transparent information and advertising standards

Various policy documents have mentioned the importance of adequate and correct information provision. The European Society of Human Genetic, for example, has stated that "labelling information on genetic tests must be true, accurate, accessible, complete and comprehensible.

Although some companies have websites providing most or all of this, the information is often of promotional nature and intended to sell tests, which might compromise the truth in labelling." (6)

Regulation of genetic tests

In the European Union, genetic tests are currently regulated by the Directive 98/79/EC on in vitro diagnostic (IVD) medical devices. This Directive was adopted in order to facilitate within the European Union an internal market for IVD medical devices and in order to make sure that such devices meet essential requirements at the level of safety and performance before market introduction. This Directive was criticized in the past among other issues for its list-based classification system lacking consistency and which required for most genetic testing only a self-certification prior to market introduction. As we explained earlier, "On September 2012, the European Commission presented a proposal for a new legal instrument after several years of public consultations. Instead of a Directive, this instrument would be a Regulation which means that this piece of legislation will be immediately binding for all Member states without a transposition into national law being necessary (European Union)." (46) The European parliament amended the proposed version of the European Commission and introduced various articles which may affect the DTC genetic testing market. The voted version of the European Parliament is currently being considered by the Council of the European Union. (47) This proposed Regulation contains a the risk-based classification of IVD medical devices, which makes of genetic tests Class C devices making premarket review by a Notified Body necessary. Amendment 72 foresees that all health-related genetic testing may only be ordered by "persons admitted to the medical profession under the applicable national legislation after a personal consultation." (48) The same amendment also provides the obligation to provide the test applicant "with appropriate information on the nature, the significance and the implications of the genetic test."(48) Furthermore, it underlines the necessity of "appropriate genetic counselling" before the provision of a genetic test, and that "the form and extent of this genetic counselling shall be defined according to the implications of the results of the test and their significance for the person or the members of his or her family."(48) Moreover, amendment 40 states that "direct to consumer advertising of devices classed as prescription only by this Regulation shall be illegal." (48) If approved, these provisions might heavily impact on the provision of DTC genetic testing.

Canalization of genetic tests through health-care professionals

In the above mentioned Proposed IVD Regulation genetic tests may only be ordered by persons admitted to the medical profession. Already at this moment various European countries foresee in their legislations that genetic tests should be ordered by physicians. This is for example the case in Germany where the German Bundestag passed on 24 April 2009 the Human Genetic Examination Act (The Genetic Diagnosis Act, GenDG), which covers genetic testing services. According to sec. 7 para. 1 of the Act, a diagnostic genetic examination may only be undertaken by physicians and a predictive genetic examination may only be undertaken by medical specialists in the field of human genetics or other physicians who have qualified themselves via the acquisition of some specialist designation for genetic examination within their specialist area. Para. 2 states that the genetic analysis of a biological sample may only be carried out within the scope of a genetic examination and by the medical person in charge or by person or institution commissioned by the responsible medical doctor. Para. 3 finally declares that genetic counseling according to sec. 10 may only be undertaken by physicians named in para. 1 and who are qualified to provide genetic counseling."(40) Also countries such as Portugal and France have legislation that foresees the provision of genetic tests through medical doctors. (40) It should however be mentioned that the provision of genetic tests through medical professionals is not a guarantee that adequate genetic counseling is being provided and that the clinical utility of genetic tests is guaranteed.

Penalization of users

In France, the French Law (Article 16-1 Civil Code) has advanced that genetic tests can only be performed with a medical prescription and by an authorised laboratory. We described the French regulation in detail in another publication. (49) The French law on Bioethics of 2011 integrated also an article that regulates the use of DTC genetic testing by consumers. (50) Anyone who is requesting a genetic test for him or herself, or for a third person, or for identification through a DNA profile, outside the conditions laid out by the law is punishable under the article 226-28-A of the criminal code by a fine of 3750 euro. We have discussed this article in detail in a previous article. "Although it is certainly defensible to elaborate such a provision in the law in order to avoid that the DNA of third parties be analyzed without their consent or that paternity testing be done without consent, it is questionable whether it is desirable that such a provision should be elaborated for prohibiting access to personal health information. The adoption of such a provision by the French legislator constitutes a serious infringement to the principle of freedom, in the name of protecting personal rights. This does not imply that personal freedom is an absolute right. The right to know must be exercised with due respect for the necessary protection of individuals. The issue of DTC genetic testing should be viewed in the general context of regulating a freedom to access, and limitation of this access, if there are doubts about the quality of the knowledge provided by these companies or if there might be risks of harmful effects for the person concerned or for public health. A regulation focusing on the prohibition of use of DTC genetic testing by consumers aims to emphasize the responsibility of individuals. In an age of internet access to genetic testing on an international scale, it also provides a warning to individuals not to order genetic tests. However, in addition to enforcement problems of such a regulation, arguments coming from the protection of Public Health are more convincing if a legislator aims to regulate DTC genetic testing. From this perspective, the French Bioethics law, which reinforces the conditions to be fulfilled for the provision of genetic testing, did not require legislation that also restricts individual freedom to obtain personal information."(50)

Penalization of non-consensual testing

Non-consensual genetic testing involves the collection of biological materials of a third person with the intention to do a DNA analysis without obtaining consent. Biological materials needed for a genetic testing can be obtained through discarded tissues, used coffee cups and smoked cigarettes left behind.(51) It has been shown that some DTC companies are not unwilling to process samples that are being submitted without proper consent. (52) Cases of 'DNA theft' and 'genetic stalking' were also reported in the literature and media. (53-57) It was re-

ported earlier that "Thwarting surreptitious genomic testing may require new laws to protect privacy by making it a crime to possess someone else's DNA with the intent to analyze it without consent."(58) In the UK, the Human Tissue Act included specific provisions that makes the procurement of some else's biological sample for DNA analysis without their knowledge a legal offence.(49)

Conclusion

Direct-to-consumer genetic testing has been heavily debated over the last years. Various professional societies and governmental bodies have issued policy statements discussing various concerns, risks and limitations. Policy reactions, however, vary. While some emphasize the importance of self-regulation of this industry and focus on some minimum criteria related to the provision of those services (transparency, truth in labelling...), others have emphasized the importance of genetic counselling and medical supervision, as well as premarket assessment of genetic tests. With the increasing amount of genetic information that can be generated at a decreasing costs, a major challenge will be how to make innovative tests accessible in diagnostics and screening, while avoiding unsound applications.(59)

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Abstract*

The paper aims to provide an overview of the most important concerns related to direct-to-consumer genetic testing and of the regulatory approaches that have been presented and/or implemented. Direct-to-consumer genetic testing has been heavily debated over the last years. Various professional societies and governmental bodies have issued policy statements discussing various concerns, risks and limitations. Policy reactions, however, vary. While some emphasize the importance of self-regulation of the industry and focus on some minimum criteria related to the provision of those services (transparency, truth in labelling etc.), others have emphasized the importance of genetic counselling and medical supervision, as well as premarket assessment of genetic tests. With the increasing amount of genetic information that can be generated at a decreasing costs, a major challenge will be how to make innovative tests accessible in diagnostics and screening, while avoiding unsound applications.

Key words: genetic tests, internet, direct-to-consumer advertising and selling, risks, limitations, regulatory policies

Abstrakt*

Práca prináša prehľad najvýznamnejších výhrad voči genetickým testom, ktoré sa poskytujú priamo zákazníkovi, ako aj prehľad regulačných prístupov, ktoré sa navrhli alebo implementovali. Genetické testy poskytované priamo zákazníkovi sa v posledných rokoch široko debatovali. Rôzne odborné spoločnosti a štátne orgány publikovali stanoviská venované rôznym výhradám, rizikám a limitáciám týchto testov. Na úrovni konkrétnych opatrení sa však prístupy značne líšia. Kým niektoré zdôrazňujú význam samoregulácie samotných výrobcov testov a sústreďujú sa na minimálne kritériá pri poskytovaní takýchto služieb (transparentnosť, pravdivé označovanie atď.), iné zdôrazňujú význam genetického poradenstva a lekárskeho dohľadu, ako aj predmarketingového hodnotenia genetických testov. So vzrastajúcim množstvom genetických informácií, ktoré je možné generovať pri klesajúcich cenách týchto vyšetrení, zásadným problémom ostáva ako zabezpečiť na jednej strane dostupnosť inovatívnych testov v diagnostike a skríningu a zároveň sa vyhnúť ich nezmyselnému používaniu.

Kľúčové slová: genetické testy, internet, priama reklama a predaj zákazníkom, riziká, obmedzenia, predpisy

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Correspondence to: Prof. Pascal Borry, Centre for Biomedical Ethics and Law, Department of Public Health and Primary Care, University of Leuven, Kapucijnenvoer 35, P.O. BOX 7001, B-3000 Leuven, Belgium, e-mail: Pascal.Borry@med.kuleuven.be

Article 7 – Individualised supervision

1 A genetic test for health purposes may only be performed under individualised medical supervision.

2 Exceptions to the general rule referred to in paragraph 1 may be allowed by a Party, subject to appropriate measures being provided, taking into account the way the test will be carried out, to give effect to the other provisions of this Protocol.

However, such an exception may not be made with regard to genetic tests with important implications for the health of the persons concerned or members of their family or with important implications concerning procreation choices.

Article 8 – Information and genetic counselling

1 When a genetic test is envisaged, the person concerned shall be provided with prior appropriate information in particular on the purpose and the nature of the test, as well as the implications of its results.

2 For predictive genetic tests as referred to in Article 12 of the Convention on Human Rights and Biomedicine, appropriate genetic counselling shall also be available for the person concerned.

The tests concerned are:

- *tests predictive of a monogenic disease,*
- *tests serving to detect a genetic predisposition or genetic susceptibility to a disease,*
- *tests serving to identify the subject as a healthy carrier of a gene responsible for a disease.*

The form and extent of this genetic counselling shall be defined according to the implications of the results of the test and their significance for the person or the members of his or her family, including possible implications concerning procreation choices.

Genetic counselling shall be given in a non-directive manner.

Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes (2008)

ETHICS OF PREVENTIVE MEDICINE
Focus on the Genetic Tests

Inge Liebaers

Center for Medical Genetics, UZbrussel,
Vrije Universiteit Brussel, Belgium

Definition

General Preventive Medicine focuses on the health of individuals, communities, and defined populations, as defined by the American College of Preventive Medicine. Its goal is to protect, promote, and maintain health and well-being and to prevent disease, disability, and death. The American College also states that in the context of public health, general preventive medicine focuses on promoting health, preventing disease, and managing the health of communities and defined populations. The practitioners combine population-based public health skills with knowledge of primary, secondary, and tertiary prevention-oriented clinical practice in a wide variety of settings.

A simpler definition, taken from the Merriam-Webster dictionary, says that preventive medicine is a branch of medical science dealing with methods (as vaccination) of preventing the occurrence of disease. Adapted to the context of this meeting it becomes: 'A branch of medical science dealing with methods – as genetic testing or genetic screening – of preventing disease at the individual or population level'.

Genetic tests

Genetic tests are procedures which directly or indirectly analyse the genome. The results can directly point to a mutation causing a disease or they can indirectly diagnose a condition by measuring the activity of a gene product like an enzyme or a metabolite not being processed because of a missing enzyme. With increasing knowledge and progress in technology, genetic tests are becoming more and more powerful in exploring our genome. Using them for individual or public health purposes, their analytical validity, clinical validity and utility as well as ethical, legal and socio-economical aspects should be taken into account. (Hastings et al. 2012, Bowdin et al. 2014)

The new genetic tests

New genetic tests are micro-array analyses to detect CNV's (copy number variants) or SNP's (single nucleotide polymorphisms) and NGS (new generation sequencing) techniques allowing WGS (whole genome sequencing) or WES (whole exome sequencing). NIPT (non-invasive prenatal testing) uses also the NGS technology. Microarray analysis allows to find out if the cause of multiple congenital abnormalities in a person are due to a deletion or duplication of a piece of DNA. Sequencing techniques allow to find gene mutations. NIPT is a performant screening test for trisomy 21 during pregnancy (Katsanis and Katsanis, 2013).

Testing versus screening

Genetic testing is requested and performed in the context of a personal or familial medical problem. Testing can occur postnatally or prenatally. The reason for the testing is to find an answer to a medical question (Sequeiros et al., 2011). The following example illustrates the different possibilities.

(1) A boy as well as his brother and maternal uncle present with a developmental delay. An X-linked fragile X syndrome is suspected. Molecular analysis of the FMR1 gene confirms the diagnosis by finding an expanded CGG repeat. The mother of the boys must be a carrier and indeed a premutation is found in the same gene. If the sister of the mother or the sister of the boys wants to know if they are carrier, they can ask to be tested. Knowing, whether they are carrier or not, is important in view of reproduction. Within the frame of genetic counseling, recurrence risks can be given and prenatal diagnosis (PND) or pre-implantation genetic diagnosis (PGD) for the condition can be discussed and performed. (Saul and Tarleton, 2012)

(2) Another example relates to pre-symptomatic testing for dominant late onset conditions like Huntingtons disease. A person, whose father or mother has the condition, has a 50 % risk of inheriting the causal mutation and develop the disease after his or her reproductive age. They may want to know in order to discuss about their reproductive choices. A pre-symptomatic test can be obtained in accordance with international guidelines. The information may be important to him or her in view of reproduction (de Die-Smulders et al, 2013).

(3) The method of choice to day to explore/find the cause of multiple malformations and mental dysfunction in a child or a foetus is CNV-micro-array. Again when a diagnosis is made, information can be given to the patient or the parents and choices can be made (Peters and Pertile, 2014).

(4) For problems such as deafness or retinitis pigmentosa, next generation sequencing can be used to find the causal mutation (Vona et al. 2014).

Genetic screening is offered in the context of a possible risk or problem in a healthy population. Genetic screening can occur postnatally or prenatally.

(1) Neonatal screening is a variably established procedure generally based on metabolite or gene-product analysis and not yet on direct gene-testing. The aim is to be able to treat as soon as possible. Genetic counseling can follow later. Screening programmes based on new genetic sequencing technologies can be envisaged. The next step could be to store the sequence 'somewhere' and interrogate/analyse this sequence whenever a health problem of that person has to be answered or when screening like for breast cancer mutations may seem appropriate. (Cornel et al. 2011, Loeber et al, 2012, Bowen et al.2012).

(2) Carrier screening based on mutation analysis for autosomal recessive conditions occurs in certain populations like Ashkenazi Jews, who are tested for Tay-Sachs disease among other specific diseases, or inhabitants of regions like Cyprus and Sicily who are tested for thalassemia because these diseases are more prevalent (Schneider et al, 2009). Testing for carriership of cystic fibrosis in high incidence populations is not yet generalized. The aim of these screening programmes is to allow couples to make reproductive choices. Screening-panels for over 300 recessive conditions do now exist and are made available by direct to consumer testing companies like Counsyl. Why not, may be the question. In any case, admitting that the analytical validity of these tests is correct, its clinical validity and its clinical utility remain to be demonstrated.

(3) Based on new genetic testing possibilities, direct to consumer screening tests for complex conditions based on incomplete research data have been offered by companies. Unacceptable as far as I am concerned because not yet ready for private or public health purposes. (van El and Cornel, 2011)

Prenatal screening during pregnancy can be invasive and specific such as testing the fetus for trisomy 21 by chorionic villus sampling or amniocentesis. Its clinical application has over the years evolved from offering it to preg-

nant women over 35 years of age to women of all ages but at increased risk based on prior non-invasive combined testing (nuchal translucency and maternal serum analysis). Today the 'non invasive prenatal test' or NIPT is increasingly proposed as a secondary (after the combined test) or primary screening test for trisomy 21, 18 and (13) (with high sensitivity and specificity) to pregnant women. If the result points to trisomy 21, still an invasive test will be performed before any termination. The question is whether with time, the NIPT may become a diagnostic test at least for trisomies. (Bianchi, et al, 2014)

In the meantime prenatal diagnosis by NIPT of some monogenic conditions has been performed. Recently the possibility of WGS by NIPT has been published (Yurkiewicz et al.2014). Prenatal screening for chromosomal aneuploidy before pregnancy that is to say, oocyte or embryo screening within the frame of assisted reproduction has been and is being offered and performed. Such preimplantation genetic screening or PGS based on counting certain chromosomes like 21, 18, 13 using fluorescent in situ hybridization (FISH) has been performed with more or less success. Limited published results, based on the micro-array technology, allowing the counting of all chromosome pairs at the blastocyst stage (day 5 after insemination) instead of the cleavage stage (day 3) claim to improve success rates in in vitro fertilization by selecting euploid embryos for transfer. (Scott et al. 2013). If not yet practically, theoretically WGS of preimplantation embryos is close by. The question is, whether to do it, when technically possible and reliable. If yes, the next question is how to choose the best embryo for the transfer? (Winand et al, 2014)

Ethics and genetic tests

Genetic tests tend to be more controversial than other medical tests although it is not always clear why.

One of the reasons is probably the fact that the result of a test may disclose a condition of another family member or may increase the risk of other family members to be at risk. One example is the presymptomatic testing for Huntington's disease and now also other late onset conditions within a family. Imagine that a grand daughter of an affected person wants to know her status but her mother doesn't want to know. If she is carrier of the disease causing mutation, her mother has to be a carrier as well. Another example is carrier testing for recessive condition at the individual or population level. If a person finds out he is carrier, the risk of his family members to be carrier as well increases.

Another reason why genetic tests may be controversial has to do with the risk that genetic information me be misused by insurance companies or employers. With the new technologies, such as micro-array analysis, whole genome, or exome sequencing, new problems or challenges arise related to the unsolicited or incidental findings also called secondary medically actionable variants (MAV's) and yet variants of unknown significance (VUS) (Bowdin et al. 2014). Discussions and clinical research projects are ongoing in order to learn how to deal with these new problems (Kullo et al 2014; Jarvik et al. 2014).

Ethical questions concerning genetic testing

If postnatal testing is performed within a family because of an existing problem in a child or an adult and a causal abnormality is found allowing to establish a diagnosis, the consequence may be that other family members are at risk to have the same condition or to have an increased risk to have affected offspring. Therefore, the family members at risk should be informed. Is this mandatory? What if the patient does not want to inform his or her family? Can or should the physician try to contact the family. The principles of beneficence, non-malficence, autonomy have to be taken into account. Sometimes the duty to inform may have to overrule privacy matters. Prenatal testing within a family should be a personal decision, be it during pregnancy or before pregnancy. Unfortunately, because of legal aspects and financial aspects which differ in countries, the availability of prenatal diagnostic procedures and preimplantation genetic diagnostic procedures are not equally available. With the technologies such as micro-array, the problem of unsolicited findings or the findings of unknown significance have arisen. In Belgium, the Centers for Medical Genetics use a consensus model, to be evaluated at regular intervals, as to how to handle the problem (Van Akker et al, 2013).

Questions to be asked concerning postnatal screening are numerous. Screening for recessive conditions is possible today and the number of diseases for which screening will be possible is increasing. Questions are related to which diseases to test for, who should offer testing, and who should pay? The discussion here is maybe more socio-economical than ethical. But how to handle genetic screening for late onset dominant conditions and complex diseases? Certainly in Europe, professionals in general are not in favor of offering these tests at the moment, but companies do or at least did. (Annas and Elias, 2014). If such tests are performed on demand by companies, tested persons may or will turn to professionals, who have to explain the meaning of the results and solve possible problems.

Questions concerning prenatal screening have always existed in the ethical debate and will remain. The main aim in screening programmes today is directed towards trisomy 21 and other less frequent non-lethal trisomies, as well as towards morphological abnormalities. Technology is available and improving, again not in an equitable way throughout Europe, unfortunately. Taking into account the analytical validity, as well as the clinical validity and utility of the NIPT, invasive prenatal screening is no longer the standard procedure. Non-invasive screening is indeed the way to go with NIPT as a secondary or even primary screening procedure next to ultrasound imaging. However, NIPT with WGS is on its way. (Yurkiewicz et al. 2014) Here a broad multidisciplinary discussion at several levels seems mandatory before application. Concerning pre-implantation screening (PGS), a difference exists between the USA and Europe. In the USA, PGS, now based on micro-array analysis, is offered to all IVF patients in some centers for reproductive medicine. They claim that IVF results improve by selecting the best possible embryo for transfer and at the same time decrease the miscarriage rates and the risk of the birth of a child with a chromosomal anomaly like trisomy 21. (Scott et al. 2013). These claims have still to be confirmed by proper studies. The next question will be concerning WGS of the embryos. Based on what is known today, I am afraid that no embryos will be left for transfer (Winand et al. 2014). If this is correct, it may be a reason to refrain from using the technology at least in a clinical setting. When used in a research setting we will learn a lot.

Pro's and con's of the new genetic tests

The new developments in genetic testing are, as said already, very valuable in research. Apart from finding more causal small deletions or duplications responsible for congenital anomalies as well as new genes and mutations in rare mostly monogenic diseases, they allow to increase the knowledge about the role of genetics in at least on-

cology, complex diseases and pharmacology. In the clinic, they are an added value if properly used for diagnostic and counseling purposes. In other words their analytical validity and clinical validity should have been evaluated and their clinical utility proven. The cost of these tests is continuously decreasing making them more easily available. At the moment the occurrence of unsollicited findings or MAV's and the findings of unknown significance or VUS are considered to be a burden. In the past it was rather exceptional to have unclear test results and time was needed to explain this to patients (Solomon, 2014). With the new tests, we expect unsolicited findings and findings of unknown significance. It is imperative to decide beforehand on the one hand which information will be made available to the patient and on the other hand ask the patient what they want to know. Next to the oral explanations, a written informed consent seems mandatory (Ormond, 2013). A way to limit unsollicited findings is by targeting the tests as much as possible which is the recommendation of the European Society of Human Genetics. However, views may differ, as exemplified by the American College of Medical Genetics, because their recommendation says that if WGS is used to solve a given problem, another 56 chosen genes should be investigated (van El et al. 2013, Green et al. 2013, Dorschner, et al. 2013). Companies, mainly USA based, have taken advantage of the new tests by offering genomic screening for health purposes based on research data still in progress. However, because of constraints, their activities have recently gone down or stopped altogether. (Annas and Elias, 2014)

Public health genomics

Many are convinced that the knowledge about our genome and the technology allowing to explore our genome better and faster will change medicine and public health. The statement may be true but the changes occur more slowly than originally thought. Maybe, it is better this way in order to be able to learn from gradual implementation of new tests based on the new knowledge. Along the same lines, one has to admit that except for some exceptions, personal medicine in general is still far away because the genome is not the only player in public or in the individual health.

Conclusion

In the field of human and medical genetics, times are very exciting for researchers and clinicians. It is fair to say that although knowledge and technology are explosive, there is still a lot to learn. Most probably, gradual implementation of the new genetic tests in the clinic and in society will allow us to cope. At the same time, we may have to refrain from using technology simply because it is available, without thinking, in a multidisciplinary manner, about the possible consequences.

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Abstract*

The paper gives an overview of the most frequent practical and ethical issues with regard to the use of genetic tests in the context of preventive medicine. Genetic tests tend to be more controversial than other medical tests, although it is not always clear why. One of the reasons is probably the fact that the result of a test may disclose a (still asymptomatic) condition in another family member or may reveal his/her increased risk. Another reason might be the supposed risk that genetic information may be misused by insurance companies or by the employers, or that it may result in other unjust discrimination or stigmatization of the individual. Several actual scenarios are discussed in the paper. With the novel methodologies of laboratory investigation, the available knowledge on genetic aspects of numerous human conditions and diseases is increasing exponentially. There is still a lot to learn, however. A gradual implementation of the new genetic tests in the clinic and in society may provide some time and mental space to cope with the overwhelming quantities of generated data and multifaceted knowledge. In the meantime, it seems important to refrain from using the new powerful technologies simply because they are available, without thinking, in a multidisciplinary manner, about the possible consequences of their hastened implementation.

Key words: preventive medicine, genetic tests, predictability, clinical validity, clinical utility, ethics

Abstrakt*

Práca poskytuje prehľad najčastejších praktických a etických problémov vo vzťahu k využitiu genetických testov v kontexte preventívnej medicíny. Genetické testy sa môžu javiť ako problematickejšie ako iné medicínske vyšetrenia, hoci nezriedka nie je dobre jasné, prečo. Jednou z príčin môže byť skutočnosť, že výsledok testu môže odhaliť (dosiaľ asymptomatické) ochorenie u iného člena rodiny alebo upozorniť na jeho zvýšené riziko. Ďalšou príčinou môže byť predpokladané riziko, že by získaná genetická informácia mohla byť zneužitá zo strany poisťovní a zamestnávateľov, alebo že by mohla viesť k nespravodlivej diskriminácii alebo stigmatizácii daného jednotlivca. Viaceré aktuálne možnosti sa podrobnejšie diskutujú v práci. S príchodom nových metód laboratórnych vyšetrení dostupné poznatky o genetických aspektoch mnohých ľudských chorôb a porúch narastajú exponenciálne. Napriek tomu však ostáva ešte veľa nepoznaného. Postupné zavádzanie nových genetických testov do klinického a širšieho populačného použitia môže poskytnúť čas a mentálny priestor, aby sa umožnilo lepšie zvládnutie obrovského množstva generovaných údajov a mnohostranných poznatkov. Medzičasom je veľmi dôležité, aby sa neponáhľalo s použitím výkonných technológií iba preto, že sú dostupné, bez predchádzajúceho interdisciplinárneho uvažovania o možných dôsledkoch ich príliš rýchlej implementácie.

Kľúčové slová: preventívna medicína, genetické testy, predpovedateľnosť, klinická validita, klinická užitočnosť, etika

**Abstracts by the editors./Abstrakty spracovali zostavovatelia.*

Correspondence to: Prof. Inge Liebaers, Center for Medical Genetics, UZbrussel, Vrije Universiteit Brussel, Kloosterstraat 47, B-1020 Brussels, Belgium, e-mail: inge@vansconsulting.be

Article 9 – Consent

1 A genetic test may only be carried out after the person concerned has given free and informed consent to it. Consent to tests referred to in Article 8, paragraph 2, shall be documented.
2 The person concerned may freely withdraw consent at any time.

Article 10 – Protection of persons not able to consent

Subject to Article 13 of this Protocol, a genetic test on a person who does not have the capacity to consent may only be carried out for his or her direct benefit.
Where, according to law, a minor does not have the capacity to consent, a genetic test on this person shall be deferred until attainment of such capacity unless that delay would be detrimental to his or her health or well-being.

Article 11 – Information prior to authorisation, genetic counselling and support

1 When a genetic test is envisaged in respect of a person not able to consent, the person, authority or body whose authorisation is required shall be provided with prior appropriate information in particular with regard to the purpose and the nature of the test, as well as the implications of its results.
Appropriate prior information shall also be provided to the person not able to consent in respect of whom the test is envisaged, to the extent of his or her capacity to understand.
A qualified person shall be available to answer possible questions by the person, authority or body whose authorisation is required, and, if appropriate, the person in respect of whom the test is envisaged.
2 The provisions of Article 8, paragraph 2, shall apply in the case of persons not able to consent to the extent of their capacity to understand.
Where relevant, appropriate support shall be available for the person whose authorisation is required.

Article 15 – Tests on deceased persons

A genetic test for the benefit of other family members may be carried out on biological samples: removed from the body of a deceased person, or removed, when he or she was alive, from a person now deceased, only if the consent or authorisation required by law has been obtained.

Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes (2008)

GENETIC TESTING FOR HEALTH PURPOSES
Regulatory Developments on the EU Level

Miroslav Mikolášik

European Parliament, Brussels (Belgium) – Strasbourg (France)

Ladies and gentlemen, dear guests,

It is my pleasure and honour to be here today. I would like to thank the organizers for invitation – especially Mrs. Lawrence Lwoff from the Council of Europe, for the good inter-institutional cooperation with European Parliament.

In my presentation, I would like to focus on the revised EU regulation in the field of genetic testing, which is covered by in vitro diagnostics, highlighting several aspects.

The current EU regulatory framework for in vitro diagnostic medical devices ('IVDs') consists of Directive 98/79/EC of the European Parliament and of the Council ('the IVD Directive'). IVDs cover a wide range of products that can be used for population screening and disease prevention, diagnosis, monitoring of prescribed treatments and assessment of medical interventions. Like Council Directive 90/385/EEC on active implantable medical devices (AIMDD) and Council Directive 93/42/EEC on medical devices (MDD), the IVD Directive is based on the 'New Approach' and aims to ensure the smooth functioning of the internal market and a high level of protection of human health and safety.

IVDs are not subject to any pre-market authorisation by a regulatory authority but to a conformity assessment which, for the majority of devices, is carried out under the sole responsibility of the manufacturer. For the high-risk devices and devices for self-testing, the conformity assessment involves an independent third party, known as 'notified body'. Notified bodies are designated and monitored by the Member States and act under the control of the national authorities. Once certified, devices bear the CE marking which allows them to circulate freely in the EU/EFTA countries and Turkey.

The existing regulatory framework for in vitro diagnostic medical devices has demonstrated its merits but has also come under criticism in recent years. In an internal market with 32 participating countries and subject to constant scientific and technological progress, substantial divergences in the interpretation and application of the rules have emerged, thus undermining the main objectives of the Directive, i.e. the safety and performance of IVDs and their free movement. This revision aims to overcome these flaws and divergences and to further strengthen patient safety. A robust, transparent and sustainable regulatory framework for in vitro diagnostic medical devices that is 'fit for purpose' should be put in place. This framework should be supportive of innovation and the competitiveness of the in vitro diagnostic medical device industry and should allow rapid and cost-efficient market access for innovative IVDs to the benefit of patients and healthcare professionals.

This proposal is adopted alongside a proposal for a Regulation on medical devices that are currently covered by the AIMDD and the MDD. While the specific features of IVDs and of the IVD sector require the adoption of a specific legislation distinct from the legislation on other medical devices, the horizontal aspects common to both sectors have been aligned.

Genetic Testing falls wihin the scope of the IVD directive revision. Many people consider the IVD medical devices regulation as the "small sister" of the Medical Devices Regulation. In the Hearing we held last year in the European Parliament one of the experts said that the IVD medical devices are not the "small sister" but the "parents" of the Medical Devices and maybe the parents of all therapies, including pharmaceutical products and surgery.

Without a proper diagnostic there is no proper treatment or prevention of diseases. Unfortunately the current directive does not assure that low quality IVD medical devices are not placed on the market. In the past there have been cases where a low quality HIV test was placed on the European market with a CE-label. A scientific institute determined already before the notified bodies approved the CE-label that these tests announced much more false negative results than other HIV tests available which means that the tests said there is no virus but in fact there is. However, this product was available for years for patients in the EU. If a blood transfusion is performed on the basis of a false negative result on HIV, this is a life-threatening risk for the recipient of the blood transfusion. Another example shows it has been reported that an expert for DNA-Tests has sent the same sample to four different laboratories and received four different results.

IVD medical devices are products that can circulate free in the common market. There are no national borders for these products in the European market. That is why it is an obligation for the European Union to ensure the highest possible safety. The proposal is based on article 114 and 168 of the Treaty. Article 114 asks for high protection of human health. Article 168, paragraph 4c gives even a specific additional legal base.

The Commission includes major improvements to address the current shortcomings of the system for IVD Medical Devices similar to those for other medical devices. The notified bodies will be substantially improved and the supervision of the member states to the notified bodies will be strengthened. Very important is that the system of market surveillance and vigilance will be strengthened. Unannounced inspections of the companies will be mandatory. Moreover, the Commission proposes to introduce a network of European reference laboratories which have an important role in the control of high-risk medical devices.

Notified bodies system

However, some further strengthening of the proposed system will enhance public safety, supervision and control over the entire certification system. Tightened provisions for the entire system concern closer supervision of the expertise that notified bodies should have inhouse as well as the subsidiaries and external experts that they use in the course of the conformity assessments they perform. A newly introduced element to the COM proposal, negotiated for both the medical devices and in vitro medical device regulations, is the introduction of an enhanced system for the highest risk classes devices, such as class D in invitro diagnostic proposal. Only special notified bodies with the requisite expertise to evaluate class D devices will be designated by the EMA to perform conformity assessment for that highest risk class of devices.

In the European Parliament, three main improvements of the commission's proposal were introduced:

1. The clinical performance study should be positively assessed by an independent ethics committee before it starts.
2. The protection of minors and other persons not able to give informed consent should be specified in the same way as in the directive of clinical trials in 2001.

3. The timelines should be moderately extended to give the ethic committee and the authorities the necessary time to assess the proposal.

The acceptability for SMEs

In the area of in vitro diagnostic medical devices many companies offering these devices are SMEs. That is why the regulation needs to take into account the capacity of SMEs to cover the burden. Of course this should not compromise health and safety. For example it should be possible to provide some requested information electronically and it needs to be specified; that the information accompanied the product shall be provided in an official union language and not in any other language. Both changes reduce the potential burden for SMEs. Translation of declarations of conformity into all official Union languages where the device is made available is a disproportionate administrative and thus cost-intensive effort, which is not justified. Like at present, availability in one Union language should be sufficient.

Classification

A completely new classification system (A-D) is proposed (A=low risk device - D=high risk device). Most stakeholders think it is appropriate and it is based on international consensus.

In-house testing

In the current directive all in-house testing, which means tests performed in a single health care institution, for example in a hospital, is exempted from the requirements. The commission proposed to keep this in principle for the risk classes A, B, C but to include them fully when tests are in class D. This needs to be slightly adapted with respect to the needs of doctors and patients in a single health care institution without dramatically changing the concept of the European commission.

Companion diagnostics

Companion Diagnostics are DNA tests that give information if a specific therapy would most lightly work in a specific patient. The huge opportunity of personalized and stratified medicine needs to be addressed properly by the regulation. The commission proposal is a good base but needs to be further clarified.

Self testing and near patient testing

Tests that are not performed by medical professionals but by patients need to be regulated even more carefully because medical professionals may include other elements of their diagnosis while laypersons may depend their decision only on the test. It is subject to criticism that the commission regulates self testing and near patient testing by medical professionals in the same way.

Informed consent

The Commission proposal focuses very much on the quality of the product. Experts and many international organisations, like the Council of Europe, OECD and the European Society for Human Genetics have again and again articulated their position that in many case even more important than the quality of the product is the framework in which the product is applied. Especially in DNA testing it is very important to respect the principle of informed consent. This has also been asked for by the European Parliament several times. A legal opinion concludes that it is possible and appropriate to introduce respective wording in the proposal. Therefore the rapporteur Mr. Peter Liese MEP proposed amendments on this issue. There is consensus that it should not be the intention of the European Union to limit the access of patients to DNA tests but appropriate genetic counselling should be offered in any case to inform about the consequences before a test is performed. To respect the principle of subsidiarity it should be left to the Members States to regulate the details and member states should have the option to go further than the regulation requires. One can even argue that it is mandatory to include informed consent in the proposal because it is a crucial element of the Charta of Fundamental Rights (Article 3) and the Charta of Fundamental Rights is legally binding for the European Union in those areas where it acts.

Ladies and Gentlemen,

I believe revision of IVD directive as adopted in the European Parliament will find support in the Council so that new legislation could be in force as soon as possible for the benefit of patients and all citizens of the EU.

Thank you for your attention.

Correspondence to: Mr. Miroslav Mikolášik MD, MEP, European Parliament, 60, Rue Wiertz, Altiero Spinelli 06F167, B-1047 Brussels, Belgium, e-mail: miroslav@mikolasik.sk

Article 12 – Authorisation

1 Where, according to law, a minor does not have the capacity to consent to a genetic test, that test may only be carried out with the authorisation of his or her representative or an authority or a person or body provided for by law.

The opinion of the minor shall be taken into consideration as an increasingly determining factor in proportion to his or her age and degree of maturity.

1 Where, according to law, an adult does not have the capacity to consent to a genetic test because of a mental disability, a disease or for similar reasons, that test may only be carried out with the authorisation of his or her representative or an authority or a person or body provided for by law.

Wishes relating to a genetic test expressed previously by an adult at a time where he or she had capacity to consent shall be taken into account.

The individual concerned shall, to the extent of his or her capacity to understand, take part in the authorisation procedure.

Article 16 – Respect for private life and right to information

1 Everyone has the right to respect for his or her private life, in particular to protection of his or her personal data derived from a genetic test.

2 Everyone undergoing a genetic test is entitled to know any information collected about his or her health derived from this test.

The conclusions drawn from the test shall be accessible to the person concerned in a comprehensible form.

3 The wish of a person not to be informed shall be respected.

4 In exceptional cases, restrictions may be placed by law on the exercise of the rights contained in paragraphs 2 and 3 above in the interests of the person concerned.

Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes (2008)

THE OVIEDO CONVENTION AND ITS ADDITIONAL PROTOCOL CONCERNING GENETIC TESTING FOR HEALTH PURPOSES

Laurence LWOFF

Bioethics Unit, Council of Europe, Strasbourg, France

The sequencing of the human genome and the development of new technologies make human genetics a very dynamic sector. Knowledge on the human genome has been a source of considerable advances, in particular the development of genetic tests enabling the identification of genetics characteristics responsible for a disease or, more frequently, involved in its development.

The results of genetic tests are sensitive personal data, which are often predictive with regard to the future health of the person concerned, and are also shared with other members of his or her biological family. These characteristics raised a certain number of concerns in particular with regard to the protection of privacy and the risk of discrimination on the basis of genetic characteristics.

These concerns have prompted the Council of Europe to focus on the ethical and legal issues raised by applications of genetics, in particular genetic testing, and to draw up legal standards to protect fundamental human rights with regard to these applications.

Protection and guarantees in the fields of biology and medicine, including human genetics, are provided by the *Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Applications of Biology and Medicine (Convention on Human Rights and Biomedicine)* (1). The Convention sets out a number of principles concerning genetics (Articles 11 to 14), particularly genetic testing and interventions on the human genome.

In order to develop and supplement the principles set forth in the Convention, a new *Additional Protocol to the Convention on Human Rights and Biomedicine was elaborated, concerning Genetic Testing for Health Purposes.* (2) This Protocol was adopted by the Committee of Ministers of the 47 Member States of the Council of Europe on 7 May 2008 and opened for signature on 28 November 2008. (3)

As underlined in the preamble of the Protocol, genetics is contributing to the progress in biomedical sciences in reducing morbidity and mortality and in improving the quality of life. Its objective is to protect against improper use of genetic testing, by providing a framework for the protection of fundamental rights and freedoms with regard to such test.

The Protocol covers all genetic testing carried out for health purposes, except those concerning the human embryo and foetus and that carried out for research purposes, which are covered by another Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research.

In the drafting of the Protocol, a certain number of issues were raised and examined, in particular: the quality of genetic testing; the capacity of analysis which keeps on increasing but is not necessarily followed by a similar capacity to act either to prevent the development of the disease concerned or to treat it; the complexity of the interpretation of the test results as well as the difficulty for the person concerned to understand all its implications; the protection of the person not able to consent; the confidentiality and security of data and samples.

The field of genetics is technically complex and constantly evolving. Different experts in genetics were consulted and the recommendations of the European Society of Human Genetics as well as the OECD guidelines on quality assurance in molecular genetic testing were taken into account.

This was particularly important for the elaboration of the provisions concerning genetic services. Article 5 on quality of genetic services, requires that genetic tests meet generally accepted criteria of *scientific validity and clinical validity*.

Particular emphasis is also placed on the importance of taking into account the *clinical utility* of genetic test as an essential criterion for deciding to offer this test to a person or a group of persons. It has to be an integral part of a good medical practice with regard to any decision to carry out a test. This was considered of particular importance for tests proposed outside any individualized medical supervision.

Information and genetic counseling as well as tests directly accessible were two issues which were particularly discussed during the preparation of the Protocol.

The Convention on Human Rights and Biomedicine requires in its Article 12 that *"tests which are predictive of genetic diseases or which serve either to identify the subject as a carrier of a gene responsible for a disease or to detect a genetic predisposition or susceptibility to a disease may be performed only for health purposes or for scientific research linked to health purposes, and subject to appropriate genetic counseling."* These requirements are reiterated in Article 8 of the Additional Protocol. The expression "appropriate genetic counseling" has been further discussed in the framework of the elaboration of the Additional Protocol. The Explanatory Report to Article 8 of the Additional Protocol specifies that genetic counseling is an individualized process taking into account, in particular, the psychological and family context of the person concerned and involving an exchange between him or her and the person providing the counseling. Genetic counseling could vary in form and extent in accordance in particular with the implications of the test and their significance for the person concerned or the members of his or her family, including possible implications for procreation choices. Genetic counseling could thus go from a "very heavy and long" procedure to a "lighter" one which may be limited to a pre-test counseling, hence the adjective "appropriate".

The quality of the prior information given to persons envisaging genetic testing, designed to enable them to take an informed decision, as well as the support provided to persons taking such decisions and dealing with the implications of a test and its results, were underlined. The Protocol thus lays down (Article 7.1) the general rule that genetic testing for health purposes may be carried out only under individualised medical supervision. Accordingly, such testing should be carried out only in response to a specific indication made on the basis of a precise evaluation, by a doctor, of the situation of the person concerned.

In this context, the issue of tests that are directly available to the individuals i.e. outside any conventional medical system, was specifically considered.

The Protocol prohibits exceptions to the general rule defined in Article 7.1 in the case of genetic testing with important implications for the health of the person concerned or his or her family members or for procreation choices.

The key concerns here are the proper interpretation of predictive tests results and the guarantee of an appropriate genetic counselling to understand its implications. The results of such genetic tests may be particularly comp-

lex to interpret and may, for instance, require that additional medical information or information about the family history be taken into account. In the case of many predictive tests, even though the test may reveal a high probability of developing a particularly serious disease, the time of onset of the disease and the severity of the symptoms are often uncertain. Lastly, the problem of understanding the nature of the test and the implications, including the implications for family members, the potential psychological impact of the results on the person concerned and the often important decisions facing that person require that such tests be carried out under individualised medical supervision.

The Protocol does, however, provide that states under certain conditions may make exceptions to the general rule in the case of tests that would not have serious implications, the principal aim being to ensure compliance with the provisions of the Protocol concerning the nature and quality of the prior information, free and informed consent and genetic counselling (Article 7.2).

Each state therefore has a degree of discretion, in the decision to allow a test to be carried out without individualised medical supervision, and when it comes to the procedures to be followed and the bodies involved in this process.

However, as the objective is to protect the person concerned, particular account must be taken of the importance of the potential implications of the test in question for the person on whom it is to be carried out or his or her family members, the ease of interpretation of the results and, where appropriate, the treatment possibilities for the disease or disorder concerned.

On that basis, the Council of Europe will continue to follow the evolution of the offer of directly accessible tests with a view to facilitating the implementation of the principles laid down in the Protocol.

With the assistance of the European Society of Human Genetics and EuroGentest, the Council of Europe has already published leaflet, which provides general objective information on genetic testing, including on their nature and the potential implications of their results. It presents the different type of tests available, their application in the medical field and the extent and limit of the significance of the information resulting from these tests. It contains a specific section on direct to consumer genetic testing. It is currently available in 29 European languages at www.coe.int/bioethics

Current activities relevant to genetics

After genetic testing for health purposes, the intergovernmental Committee on Bioethics (DH-BIO) is now working on the processing for insurance purposes of health-related data, in particular data resulting from genetic tests with a view to the elaboration of a new recommendation.

Furthermore, the DH-BIO is re-examining Recommendation (2006)4 on research on biological materials of human origin, in the light of experience acquired and developments in the field concerned since the adoption of that legal instrument.

A public consultation on a working document took place on March-August 2014. The comments received will now be analysed with a view to prepare the final version of the revised recommendation to be presented to the Committee of Ministers for adoption.

Further information on the work of the Council of Europe as well as adopted legal instruments in the field of bioethics can be found at http://www.coe.int/bioethics.

Notes and References

(1) *Convention on Human Rights and Biomedicine (Oviedo Convention) (ETS No. 164).* This Council of Europe convention was opened for signature on 4 April 1997 and has been signed by most European states. It sets out fundamental principles applicable to routine medicine and those that apply to new technology in the area of human biology and medicine. It also serves as a reference instrument for the European Union and other international organisations, such as UNESCO and the WHO. **(2)** The text of the *Additional Protocol to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes as well as its Explanatory Memorandum* can be consulted at http://conventions.coe.int/Treaty/EN/Treaties/ Html/203.htm **(3)** Lwoff, L. Council of Europe Adopts Protocol on Genetic Testing for Health Purposes. *European Journal of Human Genetics* (2009) 17, 1374–1377.

Lwoff, L. The Oviedo Convention and its Additional Protocol Concerning Genetic Testing for Health Purposes. [Dohovor z Ovieda a jeho dodatkový protokol o genetických testoch na zdravotné použitie.] Med. Etika Bioet., 21, 2014, Suppl. 1, 22-23.

Abstract*

Paper gives an overview of some of the main principles contained in the Convention on Human Rights and Biomedicine (Oviedo Convention, 1997) and its Additional Protocol on Genetic Testing for Health Purposes (2009) with regard to the ethical and legal challenges posed by the application of medical genetics, and in particular of the genetic tests in contemporary medicine and health care.

Key words: Oviedo Convention, Additional Protocol on Genetic Testing for Health Purposes, genetic tests, legal and ethical issues

Abstrakt*

Práca podáva prehľad najdôležitejších princípov obsiahnutých v Dohovore o ľudských právach a biomedicíne (Dohovor z Ovieda, 1997) a jeho Dodatkovom protokole o genetických testoch na zdravotné použitie (2009) vo vzťahu k právnym a etickým problémom, ktoré predstavuje využitie lekárskej genetiky, osobitne genetických testov, v súčasnej medicíne a zdravotnej starostlivosti.

Kľúčové slová: Dohovor z Ovieda, Dodatkový protokol o genetických testoch na zdravotné použitie, genetické testy, právne a etické otázky

**Abstracts by the editors./Abstrakty spracovali zostavovatelia.*

Correspondence to: Mrs. Dr. Laurence Lwoff, Head, Bioethics Unit, Directorate General I, Council of Europe, F-67075 Strasbourg Cedex, France,
e-mail: laurence.lwoff@coe.int

Article 17 – Biological samples

Biological samples referred to in Article 2 shall only be used and stored in such conditions as to ensure their security and the confidentiality of the information which can be obtained therefrom.

Article 18 – Information relevant to family members

Where the results of a genetic test undertaken on a person can be relevant to the health of other family members, the person tested shall be informed.

Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes (2008)

Legal Situation and Perspectives for Ratification of the Additional Protocol on Genetic Testing For Health Purposes

COUNTRIES INFORMATION[1]

ARMENIA

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* not ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes? Please specify.*

National legislations covering genetic testing for health purposes are regulated by the official Act and license of the Ministry of Health (Act No. 153: 1998; license No K-BO-66167). This Act sets out the provision on the use of genetic testing developed for medical purposes and of certain legal regulations. Regarding reasonably not large population of Armenia (approximately 3 million), the Center of Medical Genetics and Primary Health Care (CMG) is provided as a unique medical genetics service. The mandate of CMG is to support investigations on the human genome and on all aspects of human genetics related to health and diseases, including the translation of knowledge into health policy and practice, and the societal implications of genetic discoveries. The specialists of CMG perform genetic testing for molecular diagnostics of large spectrum of hereditary disorders and birth defects, male and female infertility, recurrent pregnancy loss, cancer, haematological, neurological, neuro-muscular, autoinflammatory, cardiologic diseases, including genetic counselling of patients and families and prenatal diagnostics of pregnant women. CMG carriers out the collection and storage of DNA of genetic disorders according to the bioethical laws: consent form, record the personal and medical information, and collect the blood/DNA samples with the personal barcode. Personal confidential information of thousands of persons with different genetic disorders is stored in the existing CMG Genetic Database for more accurate patient diagnosis and the associated impact on better treatment. The requirements for the development of genetic investigations, including genetic services for health care system, genetic data protection, and ethical aspects of genetic testing are regulated by the Armenian society of human genetics.

Sex selection is a huge problem in some countries, where the selective abortion has been practiced. Council of Europe could provide assistance for an exchange of views on situation in member states to facilitate the Protocol concerning the tests for health purposes, including genetic counselling, prenatal diagnostics. The assistance should be focused on educational programs for health professionals and targeted populations, considering a legislation banning gender detection before the 22nd week of pregnancy. Prenatal sex selection is indicated by a "skewed sex ratio", meaning a departure from the natural average sex ratio at birth. Resolution of the Parliamentary Assembly of the Council of Europe expressed concern over the skewed sex ratios at birth has been observed in a number of Council of Europe member states, including Armenia, where the sex ratio at birth is more prevalent for boys. Statistic shows an unnatural prevalence of boys among the children under 15 years old in some populations. Pregnant women should be offered general information about prenatal diagnostics an interpretation about health of foetus.

In 2004-2006 European Health Committee (CDSP) of Council of Europe developed the Recommendations on impact of genetics on the organization of health care services and training of health professionals (myself as the expert). Recommendation CM/Rec(2010)11 of the Committee of Ministers to member states: CDSP identified medical genetics as a medical specialty at the European level, and provided recommendation on the impact of genetics on the organization of health care services and training of health professionals in the European community. Ministry of Health of Armenia recognized Medical Genetics as a medical specialty in 2010, and in 2011 department of medical genetics was established at Yerevan state medical university; the educational program is guided by these recommendations.

3. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?*

The Convention on Human Rights and Biomedicine (Oviedo Convention) contains very important for Armenia provisions relating to genetics, including predictive genetic tests and interventions on the human genome. The ratification of this protocol must be performed by the Parliament of Armenia. The Additional Protocol concerning Genetic Testing for Health Purposes is also very important for the development of genetic service in Armenia, because the CMG serves as the only genetic institution for health purposes. As a central and beneficial deed in realization of the ratification procedure of the Oviedo convention and its additional protocol our service in medical genetics needs professional consultations and training, including participation in DEBRA conferences. Information of the additional protocol about genetic counselling seems to be very important for family doctors and other medical professionals, because it is unsufficient in the field of bioethics, newborn screening, and genetic testing of multifactorial and rare diseases. In particular, the document must be developed to cover general principles related to the functioning of genetic service in the field of reproduction to investigate the reasons of skewed sex ratios at birth, organise and support public awareness-raising conferences on prenatal sex se-lection, sex-selective abortions as common practice in some communities, particularly in case of the third or fourth child.

The Council of Europe could be very helpful in assisting in explanation of the actuality of Oviedo Convention and Additional Protocol to the Ministry of Health of Armenia (I am the chief specialist-geneticist of the Ministry of Health) and the Permanent Representative of Armenia to the Council of Europe.

Responses by: Sarkisian Tamara

Institution: Center of Medical Genetics and Primary Health Care

BOSNIA AND HERZEGOVINA

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes? Please specify.*

No. Currently, the only legislature concerning the genetic testing in Bosnia and Herzegovina is found as part of health

[1]Based on the material *Replies by country. Questionnaire for the participants at the International Bioethics Conference on Genetic Testing for Health Purposes in Central and Eastern Europe,* May 29-30, 2014, Bratislava, Slovak Republic, compiled by the Secretariat of the Committee on Bioethics (DH-BIO) of the Council of Europe. The texts contained in the Proceedings edited by J. Glasa & H. Glasová.

legislatures concerning other health issues that are in some way involving genetic testing. Therefore, at present, there is no legislature concerning only genetic testing in Bosnia and Herzegovina.

3. *If not, is it foreseen to introduce any legislation/regulations?*

Once the legal pre-requirements for the Additional Protocol concerning Genetic Testing for Health Purposes have been met, this protocol will be implemented as one form of regulation of genetic testing for the health purposes.

4. *If your country has ratified the Oviedo Convention, but not it's Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?*

Bosnia and Herzegovina signed (16.12.2005.) and ratified (11.05.2007) the Council of Europe Convention on the Protection of Human Rights and dignity of the human being with regard to the Application of Biology and Medicine (Oviedo Convention) and the Additional Protocol on biomedical research.

During the meeting of the Committee on Bioethics (DH - BIO), the Council of Europe, held in Strasbourg on 19-22 June in 2012, Bosnia and Herzegovina was encouraged to start the procedure for signing the additional protocols to the Convention (Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin; Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes; and Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings).

Out of those three, only the last one (the Prohibition of Cloning Human Beings) has received full support from the competent health authorities in Bosnia and Herzegovina, while for the other two (concerning transplantation and genetic testing) legal pre-requirements have not been met as yet.

The Council of Ministers of B&H on its 72nd Session held on 28 November 2013, adopted and the Presidency of B&H on its 45th Session held on 26 March 2014, endorsed the Decision on acceptance of the Additional Protocol to the Council of Europe Convention on the Prohibition of Cloning of Human Beings. The Protocol will be signed soon by the empowered Ambassador of Bosnia and Herzegovina to the Council of Europe.

Hence, the Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes still remains unsigned.

5. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?*

Consultations, trainings and workshops on ratification and implementation of the Protocol concerning Genetic Testing for Health Purposes for the competent authorities in B&H.

Responses by: Nina Maric (1), Aida Saracevic (2)

Institutions: (1) Clinical Center Banja Luka, (2) Centre for Genetics, Medical Faculty, University of Sarajevo

ESTONIA

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes?* No.
3. *If not, is it foreseen to introduce any legislation/regulations?* Data not available.
4. *If your country has ratified the Oviedo Convention, but not it's Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?* Taken into the agenda.
5. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?* None.

Responses by: Vaike Leola

Institution: Estonian National Bioethics Committee

LATVIA

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes? Please specify.*

The Human Genome Research Law ((hereinafter – the Law), from 13th of June 2002, valid from the 1st of January 2004) and the Regulation of the Cabinet of Ministers of the Republic of Latvia No.692 "Procedures for Genetic Research" (adopted on 10 August, 2004) are the main regulations in Latvia covering genetic testing. In addition to these regulations we have another regulation on genetic scope.

- The Law defines the general principles of human genome research, emphasizing that in genetic research the interests, rights and protection of a gene donor shall be set higher than the interests of society and science.
- The purpose of the Law is to regulate the establishment and operation of the single genome database of the State population (hereinafter – genome database) and genetic research, to ensure the voluntary nature and confidentiality of the gene donation in respect of the identity of gene donors, as well as to protect persons from the misuse of genetic data and the discrimination related to the genetic data.

  The Law regulates:

  – the provisions for the tissue sample processing, preparation of the description of the DNA, description of the state of health and genealogy in relation to the genome database;

  – the genetic research regulations in relation to the genome database and organization of the supervision of such research;

  – the rights and obligations of gene donors, activity of the chief processor, authorized processor of the genome database and gene researchers;

  – the restrictions in relation to the use of tissue samples, the use of descriptions of the DNA compiled in the genome database, descriptions of the state of health and genealogy;

  – coding and decoding provisions.
- The Law prescribes that the gene donor participates voluntarily in the genetic research. It is prohibited to discriminate against a person in relation to his or her genetic origin and any other data acquired as the result of the genetic research, as well as on the basis of the fact that the person is or is not a gene donor.
- The Law prescribes that genetic research is permitted for the purpose of studying and describing the mutual connection between genes, the human state of health, lifestyle and physical and social environment, in or-

der to discover, on the basis of such research, disease diagnostic and treatment methods that will help to assess the health risks of the individuals and to prevent the causes of diseases.

- Genome research of a deceased person may not be performed if this is against his or her expressed will while alive. If such a will was not expressed, it is prohibited to perform the genome research of the deceased person.
- The Law defines the Consent to Become a Gene Donor and Rights of Gene Donors, for example, before a person participates in the genetic research, a doctor shall issue to the person written information regarding:
  - the purpose, content and duration of the genome research project;
  - potential risks;
  - the right to freely express his or her consent and to revoke it at any time;
  - a possibility to perform genetic research outside of Latvia;

The consent of a person to take tissue samples from him or her, to prepare and supplement the description of the state of health or the genealogy, to include such description in the genome database and use it in the genetic research and for the purpose of statistics, to bring it out of Latvia, as well as to use the genetic data shall be provided in writing. The consent document of a gene donor shall be prepared in two copies; the document shall be signed and dated by the gene donor or his or her guardian or trustee and the chief processor or the authorized processor. One copy of the consent document shall be kept in the State Population Genome Register; the other copy shall be issued to the gene donor or his or her guardian or trustee.

- The State Population Genome Register shall keep the consent document of a gene donor for 75 years after the last entry characterizing the tissue samples, the description of the state of health and the description of the DNA.
- The Law also describes the Operations with Tissue Samples, Descriptions of the State of Health, Genealogies, DNA Descriptions and Personal Data of the Gene Donor as well as Requirements for Coding and Recoding and Supervision and Procedures for Examination of Complaints.

We have established the Single Genome Database in 2006. The chief processor of the genome database is Latvian Biomedicine Research Institute. The tasks of the chief processor are following:

- to organize the taking and storage of tissue samples, the preparation, storage and destruction of descriptions of the state of health and genealogies;
- to perform the coding;
- to perform the genetic research and to collect, store, destroy or issue the genetic data;
- to provide the State Population Genome Register with the genetic data acquired as the result of the genetic research related to a particular gene donor;
- to promote the development of genetic research in Latvia; and
- to promote the utilization of the results of the genetic research for the improvement of health of the person and the whole of society.

- If the genetic research is performed irrespective of the genome database, the information regarding the state of health of the person, tissue samples and descriptions of the DNA shall be included in the genome database only upon a written consent of the gene donor. In such case, a gene researcher has the right to work with the tissue samples, which he or she has collected and stored in a ge-nome database, within the scope of their powers as prescribed by the Law.
- The full text of the Law in English is available at: http://www.vvc.gov.lv/export/sites/default/docs/LRTA/Likumi/Human_Genome_Research_Law.doc
- The Regulation of the Cabinet of Ministers of the Republic of Latvia No.692 "Procedures for Genetic Research" (adopted on 10 August, 2004)
- The Regulations determines the procedures for genetic research and the documents that must be provided to allow the launch of genetic research (the positive opinion of the Genome Research Council and the positive opinion of the Central Medical Ethics Committee). The Regulations prescribes that in the genetic research only coded tissue samples, coded descriptions of DNA, coded state of health may be used.

3. *If your country has ratified the Oviedo Convention, but not its Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?*

Latvia has ratified the Oviedo Convention. Currently Latvia has started work on the ratification of the Additional Protocol concerning Genetic Testing for Health Purposes. We have evaluated the national legislation on genetic testing. It is planned to ratify the Additional Protocol in the near future.

Responses by: Ēriks Miķītis

Institution: Ministry of Health of the Republic of Latvia

LITHUANIA

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes? Please specify.*

- National standards for genetic counselling and pro fessional responsibilities of clinical geneticists are regulated by the Act No. V-220/2003 of the Ministry of Health.
- Specific requirements for the provision of genetic services (i.e. the requirements for the specialists providing genetic services, premises, medical devices and other medical equipment, organization of provision of this services) are established in 2012 (Act. No. V-745/2012 of the Ministry of Health).
- Genetic services are a part of the Lithuanian health care system. They are paid by the National health insurance fund under certain medical indications, listed in 2005 (Act. No. V-522/2005 of the Ministry of Health).
- Universal newborn screening for inherited metabolic diseases is performed following the procedure established in 2004 (Act No. V-865/2004 of the Ministry of Health).

3. *If your country has ratified the Oviedo Convention, but not its Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?*

- There might be an uncertainty with regard to implementation of some provisions of the Protocol, particularly with regard to the provisions of the Article 5, Article 8, since according to Kucinskas et al, there is a relatively low number of specialists providing gene-

tic services for the population of Lithuania in comparison to the leading West European countries. Also there is an absence of standards and appropriate training for the specialty "medical geneticist"; graduate non-MD medical geneticists must be further trained at their working place, but there are no system and budget for such training.

4. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?*

Similar conferences as the one being organized now would help to increase the awareness of the Protocol as well as to facilitate progress towards the ratification procedure.

Responses by: Jurate Lekstutiene

Institution: Lithuanian Bioethics Committee

MOLDOVA

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes? Please specify.*

Law Nr. 1256 from 19.07.2002

http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=352146

3. *If your country has ratified the Oviedo Convention, but not it's Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?*

Partly, containing of Additional Protocol, referring to research on embryos and cloning of human is reflected in the Law Nr. 138 from 15.06.2012,

http://lex.justice.md/index.php?action=view&view=doc&lang=1&id=344838

4. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?*

The representatives of CoE to come and work in a team with representatives of the Ministry of Health of Moldova, local legal authorities and genetic researchers.

Responses by: Natalia Usurelu

Institution: Institute of Mother and Child, Centre of Reproductive Health and Medical Genetics

MONTENEGRO

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* ratified on March 19, 2010.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes?*

There are several laws in Montenegro, which cover different aspects of genetic testing for health purposes:

- The Law on genetic data protection (Published in "Official Gazette of Montenegro", no. 25/2010, www.mzdravlja.gov.me).
- The Law on collection and utilization of biological samples (published in the "Official gazette of Montenegro, no. 14/2010, www.mzdravlja.gov.me)
- The Law on Infertility Treatment with Assisted Reproductive Technologies (published in the "Official gazette of Montenegro", no. 74/2009, www.mzdravlja. gov.me)
- The Law on the conditions and procedures for artificial termination of pregnancy, 27 July 2009.
- The Law on removal and transplantation of human body parts for the purposes of medical treatment (published in the "Official gazette of Montenegro", no. 76/2009, www.mzdravlja.gov.me)

The Law on genetic data protection

The Law on genetic data protection plays the central role regarding the most important medical and ethical aspects of genetic testing use, with respect to protection of the most important human rights regarding genetic testing.

The crucial reasons for passing the Law on genetic data protection were: demand of regulating the collection, use, processing and storage of human genetic data and samples, with special focus on protection of privacy, dignity, integrity, identity and other personal rights and freedoms; necessity to regulate conditions for the genetic testing procedures - performed only for diagnostic, predictive, preventive and therapeutic purposes; need to prevent discrimination and stigmatization against an individual, family, or community groups, due to their genetic traits known by genetic testing.

The Law on the protection of genetic data is consistent with the International/European legislation:

- Convention on Human Rights and Biomedicine,
- Additional Protocol to The Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes - adopted by the Council of Europe and
- International Declaration on Human Genetic Data,
- Universal Declaration on Human Genome and Human Rights,
- Universal Declaration on Bioethics and Human Rights - adopted by UNESCO.

General provisions and aims of this Law refer to:

- collecting, using, processing and storage of human genetic data and samples, obtained by genetic testing and analysis performed for health purposes,
- genetic testing and genetic analyses conducted within genetic investigations in people, including prenatal genetic investigations of embryo and foetus during fertilization and pregnancy;
- protection of identity, privacy, respect for human dignity personal integrity, equality, free decision and self-determination, including the right to genetic informing and counselling prior to, and after the conducted testing;
- determination of the terms of references for medical institutions and medical professionals, ensuring appropriate quality of genetic services (genetic testing and genetic informing and counselling), consistent with bioethical recommendations and directives.

Provisions of this Law do not refer to determining paternity or maternity, as well as to the scientific research work.

Genetic pretesting information, written consent and genetic counselling and reporting the results after performing genetic testing are mandatory actions and have to be conducted by responsible doctor in written form.

Law on genetic data protection demands compulsory evidence and registries of medical institutions, that perform genetic testing and collecting of genetic data and samples, and also demands regulatory bodies monitoring and evaluation.

The other, **above mentioned Laws** cover different aspects of genetic testing, such as gender sensitive issues and clearly prohibit genetic testing and consecutive prenatal sex selection, except for health purposes:

- "After prenatal genetic testing it is not allowed to inform

future parents about sex of embryo, before the completion of 12th week of pregnancy. Exception is for the prenatal genetic testing when sex determination for medical purposes is indicated by responsible medical doctor (clinical geneticist)." - Law on genetic data protection.

- "It is not permitted to conduct prenatal genetic testing in early pregnancy (up to 10 weeks of gestation), to sex determination, except when there are sex related risks for genetic disorder, indicated by clinical geneticist." - Law on the conditions and procedures for artificial termination of pregnancy.
- Law on the treatment of infertility, with assisted reproductive technologies, prescribes the obligation of medical institutions that conduct assisted reproduction technologies to form the Medical Board, including medical doctor certified in medical/clinical genetics, as a mandatory member.

3. If your country has ratified the Oviedo Convention, but not it's Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?

Montenegro has ratified Additional Protocol concerning Genetic Testing for Health Purposes on 12 February 2013.

4. If your country has already ratified the Additional Protocol, what assistance could the Council of Europe provide to facilitate its implementation?

The ratification of Convention on Human Rights and Biomedicine (Oviedo Convention) and its Additional Protocol concerning Genetic Testing for Health Purposes, and also passing of several national laws and regulations, that cover genetic testing for health purposes, present a good framework for human rights protection in the field of biomedicine.

Regarding Montenegro population characteristics (population of approx. 670.000, multiethnic, life expectancy 73/76 years man/women respectively, live births approx. 8000/year, infant mortality rate < 6/1000), medical genetics service in Montenegro is provided as a unique centralized service at the tertiary health care level in the Clinical Centre of Montenegro. Centre for medical genetic and immunology at the Clinical Centre of Montenegro provides genetic service including clinical genetics, register of genetic diseases, prenatal and postnatal genetic testing for most common genetic disorders, pre- and post-testing genetic counselling.

Principles of genetic testing, informing and counselling are based on contemporary bioethical statements and Convention on Human Rights and Biomedicine (Oviedo Convention) and its Additional Protocol concerning Genetic Testing for Health Purposes. Within medical genetics service all patients in need of genetic testing are provided with pretesting counselling and written information, written consent, genetic testing results interpretation, post-testing genetic counselling and written genetic information, comprehensible and non-directive counselling that are provided ex-clusively by a medical doctor - clinical/medical geneticist.

Several laws which have been passed a few years ago, and experiences from the activities in the field of medical and clinical genetics in Montenegro made an appropriate ambient for further goals in the field of bioethics, but some pending issues still exist. Rapid "genetization" of medicine requests our presence, alertness and quick response in protecting against any misuse of genetics achievements and in defending human rights. Accumulated knowledge under lines the need to promote ethical aspects connected with genetic testing and research, as well as necessity for better education of medical professionals and general population, preparing them for appropriate social and legal response to the emerging ethical issues.

Common knowledge about medical genetics and genetic testing for health purposes within the general population still seems to be insufficient in Montenegro. Also general practitioners, family medicine doctors and other medical professionals, who are not involved in medical genetic services, need better education due to recent advances in the field of medical genetics and genetic testing. Furthermore, spreading of private medical services, which are not always integrated in the national health system, has brought a different approach and genetic knowledge implementation in the field of genetic testing for health purposes, not always consistent with the national Law.

Future actions should be undertaken to provide complete coverage of Law implementation, focusing on:

- promotion of genomic health and bioethics in the field of medical genetics;
- investigation on general population and medical professionals regarding the knowledge and attitudes toward genetic testing and bioethical issues;
- developing the "behaviour change communication strategy" to prevent misuse of genetic testing and to avoid prenatal sex selection in private medical institutions, and in the neighbouring countries;
- developing educational programs and organizing education in the field of bioethics focused on medical professionals and general or targeted population;
- provision the quality of genetic services, pre- and post-testing genetic counselling and prenatal diagnostics, and alignment the medical genetics and bioethics standards;
- development of regulatory bodies activities toward continuous monitoring and evaluation of human rights protection in bioethics;
- spreading regional integration and cooperation.

Possible Council of Europe assistance could be focused on the support of several activities/areas:

- expertise for promotion of ethical aspects of genetic testing and research, especially for prenatal and preconception genetic testing, genetic counselling and of genomic health;
- expertise for investigation on general population and medical professionals regarding knowledge and attitudes toward genetic testing and bioethical issues;
- expertise for developing "behaviour change communication strategy", regarding changing attitudes towards prenatal sex selection among general population, but also among medical professionals;
- organization of regional round tables and conferences with the purpose of exchanging experiences in the field of preparation and implementation of legislation regarding genetic testing for health purposes;
- support in the education and training of medical and other professionals in the field of bioethics.

Responses by: Olivera Miljanovic

Institution: Centre for Medical Genetics and Immunology, Clinical Centre of Montenegro, Medical Faculty, University of Montenegro

SERBIA

1. Convention on Human Rights and Biomedicine (Oviedo Convention): ratified.

2. Does your country have any legislation or regulations covering genetic testing for health purposes? Please specify.

The only legislation concerning genetic testing in Serbia is found as a part of the health legislatures concerning other health issues, as the Law on Health Care and the Law on Infertility Treatment using procedures of medically assisted fertilization. Serbia has detailed prescriptions on professional education and training of medical professionals (medical doctors) in the discipline of medical genetics. Serbia do not have clinical genetics specialization at the University of Belgrade, but introduced laboratory medicine, which lasts four years, and students will learn clinical genetics. Laboratory professionals work in eight public and in three private genetics laboratories.

3. *If your country has ratified the Oviedo Convention, but not it's Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?*

The ratification of Convention on Human Rights and Biomedicine (Oviedo Convention) cover some issues in genetic testing but the Additional Protocol Concerning Genetic Testing for Health Purpose has to be ratified in order to have a good framework for the protection of human rights in the field of biomedicine. Common knowledge among medical doctors, other medical professionals and general public in Serbia about medical genetics and genetic testing needs better education due to the advances in the field of biomedicine. Serbia has to establish national reference laboratory for all specific issues in genetic testing with the well-educated staff, adequate space and equipment.

4. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?*

We need assistance, consultations/workshops for the medical professionals and competent authorities. Organization of regional round tables with a purpose of exchanging experience in the field of bioethics.

Responses by: Nada Vasiljevic

Institution: Direction of Biomedicine, Ministry of Health of Serbia

SLOVAKIA

1. Convention on Human Rights and Biomedicine (Oviedo Convention): ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes? Please specify.*

Slovak Republic (Slovakia) does not have a specific legislation on just genetics testing for health purposes as such, but her extensive legislation framework of health, health care, and health care system legislation (in particular the Law No.576/2004 Coll. on health care, and Law. No. 578/2004 Coll. on health care providers, both as later amended); data protection legislation (Law. No. 122/2013 Coll. on protection of personal data (superseding previous law on the same subject)); human rights protection legislation; family and citizens legislation are applicable as appropriate also to the area of genetic testing for health purposes, including for biomedical research and drug clinical trials. More detailed analysis is beyond the scope of this questionnaire.

Slovakia posses also detailed legislation and related prescriptions on professional education and training of medical professionals (medical doctors) in the discipline of medical genetics, as well as outlining the necessary conditions for practicing medical genetics within the Slovakia's health care system. The same holds for the laboratory professionals in genetics laboratories.

Slovakia has a specific Law No. 417/2002 Coll. (as later amended) on the use of DNA for the identification of persons.

Slovak Society of Medical Genetics (SSMG), branch of the Slovak Medical Association, issues professional guidelines for her members and for the medical genetics centres and laboratories in Slovakia. The latest version of the "Principles of genetic testing" was issued by the SSMG Board on March 2, 2012. It builds upon and cites important international guidelines and other instruments in the field, including the UNESCO declarations, European Commission's 25 recommendations, European Society of Human Genetics (ESHG) recommendations on genetic testing, Slovakian Constitution and applicable legislation (in general), as well as the documents of the Council of Europe: Oviedo Convention (1997), Additional Protocol on Genetic Testing for Health Purposes (2008), and the CoE's Recommendations: Rec. (90)13, Rec. (92)3, Rec. (97)5 and CM/Rec.(2010).

3. *If not, is it foreseen to introduce any legislation/regulations?*

When drafting the extensive new health, health care and health care system legislation in 2003 – 2004, more detailed provisions for several areas of biomedicine were proposed and debated, including e.g. more detailed provisions for human genetics, human assisted reproduction, bio-banks, cloning etc. As the necessary political consensus was not reached at that time, the "problematic" ("controversial") provisions were deleted from the legislation at that time for the sake of its passing through the parliament.

Within the accession process of Slovakia to the European Union, several legislation provisions had to be introduced to make for the required compatibility of the Slovakian with the EU law. This surely included also some provisions applicable to genetic testing field. After entering EU, Slovakia has to comply also with all EU legislation, as required/agreed, including application of the respective Directives into her legal system, and complying with the directly applicable Regulations as well.

It is my guess that when health, health care legislation is opened for more extensive amendments in the (near/more far?) future, the questions/issues cut away within the 2003-2004 legislative processes will surely pop-up again, especially because already at present the voices from professional community point out the necessity of such legislation changes/provisions. I do not think, however, such legislative initiatives are to be expected within the present parliament's term, i.e. before the next future elections in Slovakia (2016).

4. *If your country has ratified the Oviedo Convention, but not its Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?*

There are no real obstacles, as it is understood that via its CDBI/DH-BIO delegation Slovakia took a direct part in the elaboration processes of the Protocol. It is also understood that the Protocol is not at all contrary to any provision in the applicable Slovak law. However, the ratification is not seen as a strong priority at present, while the Ministry is being busy with other tasks. The Additional Protocol on Transplantation has been recently pushed into the ratification process. I believe the Additional Protocol on Genetic Testing for Health Purposes should normally follow rather soon.

5. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?*

I believe that hosting of this DEBRA Program conference,

specifically devoted to the AP on Genetic Testing for Health Purposes, by the Ministry of Health of the Slovak Republic, even at the Ministry's premises, with foreseen participation/attendance of the Ministry's officers and leadership, may really help to appreciate the benefits of ratification, and put the process into an appropriate movement. The necessary momentum might also be enhanced by the participation of the experts/real life workers in genetics from Slovakia, providing a good opportunity for discussions with colleagues from other CEE countries, as well as discussion among the Slovakian participants themselves, hopefully leading to a clear underscoring the importance of the early on ratification.

6. *If your country has already ratified the Additional Protocol, what assistance could the Council of Europe provide to facilitate its implementation?*

Slovakia has not yet ratified this AP.

I do believe that after some ratifications are completed in some more countries within CEE area, similar DEBRA meeting could be organized in one of CEE countries specifically devoted to the problems/challenges of the AP implementation. Slovakian authorities might be interested again to host such conference.

Responses by: Jozef Glasa

Institution: Slovak Medical University in Bratislava: Institute of Health Care Ethics, Institute of Pharmacology and Clinical Pharmacology; Institute of Medical Ethics and Bioethics n. f.; Bratislava

SLOVENIA

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes?*

At this point there is no national legislation or regulations.

3. *If not, is it foreseen to introduce any legislation/regulations?*

Yes, it is in the phase of preparation.

4. *If your country has ratified the Oviedo Convention, but not its Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?*

Slovenia ratified the Additional Protocol.

5. *If your country has already ratified the Additional Protocol, what assistance could the Council of Europe provide to facilitate its implementation?*

– regulation in the field of direct to consumer genetic testing,

– following/promoting strict rules about genetic testing and counselling – who is competent (?),

– public actions? informing lay public?

Responses by: Luca Lovrecic

Institution: Clinical Institute Of Medical Genetics, University Medical Center Ljubljana

TURKEY

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes?*

Regulation of the Diagnostics Centres for Genetic Diseases.

This regulation covers; the diagnosis centres which apply pre-natal and/or post-natal methods for genetic diseases, those public institutions and organizations, and private legal entities and people who run the said diagnosis centres, and their activities as well. In the scope of this regulation, the health related tests only can be carried out, and a consent form is requested for each test from the patient. Genetic counselling is provided for each patient. Test results are delivered to the patient only, and not saved to the health database.

3. *If your country has ratified the Oviedo Convention, but not its Additional Protocol concerning Genetic Testing for Health Purposes, what are the current possible obstacles to this ratification?*

The assessment process regarding the above mentioned additional protocol is still continuing in consultation with the scientists from the universities in our country.

4. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?*

At present, we have no request from the Council of Europe for any assistance in this regard. We would like to express our appreciation for their previous support.

Responses by: Demet Tass

Institution: The Ministry of Health of Turkey

UKRAINE

1. *Convention on Human Rights and Biomedicine (Oviedo Convention):* not ratified.
2. *Does your country have any legislation or regulations covering genetic testing for health purposes? Please specify.*

Yes. Regulations for genetic testing for infertile couples, women with miscarriages etc.

3. *What assistance could the Council of Europe provide to facilitate progress in your country towards the ratification procedure?*

The ratification procedure strongly depends on the Parliament of Ukraine. Many times Oviedo Convention was submitted for consideration, but strong lobby cancelled it. Ukraine needs well prepared information campaign all over the country. When people will understand the content and importance of the Convention and its Additional Protocols, then it will be impossible to decline the ratification. Right now, the problems of bioethics are not understood by the common people in Ukraine.

Name: Natalya Silina

Institution: Department of Medical and Psycho-Social Problems of Family, Institute of Pediatrics, Obstetrics and Gynecology

Article 20 – Public information

Parties shall take appropriate measures to facilitate access for the public to objective general information on genetic tests, including their nature and the potential implications of their results.

Article 22 – Wider protection

None of the provisions of this Protocol shall be interpreted as limiting or otherwise affecting the possibility for a Party to grant persons concerned by genetic testing for health purposes a wider measure of protection than is stipulated in this Protocol.

Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes (2008)

CONCLUSIONS OF THE ROUND TABLE

Participants wanted to highlight following points coming out from their discussions and sharing of information at the conference about respective challenges in their countries with regard to the genetic tests for health purposes, especially concerning health policy and ethical issues involved, as well as the needs of even a better protection of human dignity, fundamental rights and respective interests of their citizens, when implementing these novel, powerful tools in everyday's medicine and health care.

1. Participants found the exchange of information on the realities of respective situations in the area of genetic tests conducted for health purposes in their countries particularly useful and interesting. Besides understandable differences, many similarities among their respective situations, understanding of existing deficiencies and shortcomings, emerging needs and perspectives, as well as the novel, common challenges, were identified. Within the laudable efforts, witnessed in the countries of Central and Eastern Europe, being aimed at an appropriate, useful and safe application of genetic tests and medical genetics services, following points might be of particular practical interest:

- organization of genetic services to improve efficiency – in terms of pooling precious resources – material, equipment and expertise, by their appropriate centralization;
- regional collaboration between countries to rely on specific expertise to cover broader necessary spectrum of the genetic services;
- private – public dichotomy of genetic services: issues of quality, equity of access, privacy and other individual concerns protection;
- education and training – some serious gaps exist; there is a strong need for appropriate capacity building – training of the expert health personnel, especially for genetic counselling; having an internationally recognized, harmonised curriculum in medical genetics may be useful;
- education, information of the general public and of the health care professionals, doctors in general (i.e. of the "non-geneticists") need to be improved and should include the relevant ethical and legal aspects;
- patients driven developments are to prevail in the closer future – probably not so much those of the technology driven; an appropriate balance should be sought and achieved, however, between the real needs and possibilities, including sustainability, to adequately address and meet the needs of the patients and of the society, while dealing effectively with the false hopes and unrealistic hypes introduced within the boom of an unrestricted commercialization;
- legal situations might be characterized by some gaps here and there, but even a more pressing problem seems to be the effective implementation and enforcement of existing – and forthcoming legal provisions in real life practice; while still not having effective enough and reliable control mechanisms in place that would be able to provide the necessary oversight;
- genetic tests offered by private companies, sometimes well-hidden from an official oversight, the phenomenon that is increasing at a great speed, including direct-to-consumer advertising and selling via Internet, still characterized by a very speedy evolution of technologies; hereby, insufficient or inadequate, or none consultation services are available; this may substantially increase the risks of potentially serious consequences for the lay customers/users/patients; also the protection of privacy could be an issue in such poorly controlled commercial settings;
- strong markets exist, and still grow, for genetic testing (too frequently without proper counselling possibilities), therefore, having a proper legislation in place may help to prevent potentially serious future problems (those in the respective health policy, medical, ethical and legal realms).

2. Participants acknowledged several perceived benefits of the prospective ratifications of the *Additional Protocol to Oviedo Convention concerning Genetic Testing for Health Purposes* by their respective countries, especially from the point of view of positive and more streamlined developments of their countries' own legislations, currently rather under-developed in this area. In the countries, where ratification of the *Oviedo Convention and its Additional Protocols* had been in a more active progress, the positive influence upon the national legislation development and implementa tion may be documented. The participants also stressed the need for closer work with their state authorities, and parliaments, to enhance and speed up the ongoing, or still just planned, ratification processes. In these efforts, positive activities, channelled by appropriate Council of Europe structures, might be very helpful.
3. Participants noted a relatively frequent lack of political and public interest, experienced in their countries, sometimes caused by a low, or inadequate public, or even professional awareness and education levels, as well as by some specific characteristics of the national legislation systems and processing, as main reasons for somewhat delayed and slow ratification progress concerning the *Convention and the Additional Protocols* in general, and the *Additional Protocol concerning Genetic Tests for Health Purposes* in particular. In this respect, awareness building and more effective information and educational activities at the national levels, possibly with an international (or international - regional) input and support seem to be both useful and necessary.
4. The usefulness and importance of regional conferences, such as the one just held in Bratislava within the Council of Europe DEBRA Program, was gratefully acknowledged and underlined. It is necessary to provide an adequate political and economic support for similar endeavours in the future. Despite the "regional" international aspects are of utmost importance for the present and for the near future time being, input providing truly European, or even broader (global) international perspective (as was the case also with the contributions of the internationally renowned invited speakers at this conference), does seem to be equally, and even increasingly important.

Based on the compilation of the delegations' interventions collected during the roundtable discussions held during the second day of the conferenced, i.e. on May 29 – 30, 2014.

Edited by Jozef Glasa.

Correspondence to: Prof. Jozef Glasa, MD, PhD, PhD, SLOVAK MEDICAL UNIVERSITY IN BRATISLAVA, Limbová 12-14, 833 03 Bratislava, Slovak Republic, e-mail: jozef.glasa@szu.sk

International conferences in Bratislava sponsored by the Council of Europe

Medzinárodné konferencie v Bratislave podporené Radou Európy

(1992 – 2014)

- Regional Czecho-Slovakia - Hungary - Poland Symposium – Contemporary Problems in Medical Ethics, Bratislava, January 3-4, 1992 (P)
- Council of Europe Conference – Teaching of Bioethics in Europe, Bratislava, November 23 - 25, 1993
- International Course in Bioethics and International Bioethics Conference – Health Care under Stress – Maintaining Integrity in Time of Scarcity , Bratislava, August 26 - 31, 1996 (with the Information and Documentation Centre on the Council of Europe, Bratislava) (P)
- International Conference – Convention on Human Rights and Biomedicine, June 25 – 26, 1999 Bratislava (on the occasion of the 50th anniversary of the Council of Europe) (Program DEBRA)
- International Bioethics Conference – Ethics Committees in Central & Eastern Europe, Bratislava, October 26 – 27, 2000 (Program DEBRA) (P)
- International Bioethics Conference – Ethics of Human Genetics: Challenges of the (Post) Genomic Era, Bratislava, October 23 – 24, 2002 (Program DEBRA) (P)
- International Conference – Clinical Ethics Support, Bratislava, November 18 – 19, 2004 (Program DEBRA) (P)
- 8th Conference of the Ministers of Health of the Council of Europe Member States – People on the Move: Challenges for Health and Human Rights, Bratislava, November 22 – 23, 2007 („Bratislava Declaration on Migration, Health and Human Rights“ adopted)
- Council of Europe Regional Conference – Oviedo Convention in Central and Eastern European Countries, Bratislava, September 24 – 25, 2009 (on the occasion of the 60th anniversary of the Council of Europe and the 10th anniversary of the entry into force of the Oviedo Convention) (Program DEBRA) (P)
- Regional International Bioethics Conference – Genetic Testing for Health Purposes in Central and Eastern Europe, Bratislava, May 29 – 30, 2014 (Program DEBRA) (P)

(P) – Proceedings published.

Medicínska etika & bioetika - Medical Ethics & Bioethics. Medzinárodný, dvojjazyčný, vedecko-odborný časopis pre otázky medicínskej etiky a bioetiky. Je určený najširšej medicínskej a zdravotníckej verejnosti v Slovenskej republike a v zahraničí, zvlášť členom etických komisií. Má za cieľ napomáhať medzinárodnú výmenu informácií a dialóg na poli medicínskej etiky a bioetiky. Prináša informácie o aktuálnych podujatiach a udalostiach v oblasti medicínskej etiky a bioetiky, pôvodné práce, prehľady, významné materiály a dokumenty, kurz pre členov etických komisií, listy redakcii a recenzie. Pôvodné vedecké a odborné práce publikované v časopise sú recenzované a musia zodpovedať obvyklým medzinárodným kritériám. Založený v roku 1994 Nadáciou Ústav medicínskej etiky a bioetiky. Počas prvých rokov existencie tvorba časopisu nadväzovala na vedecko-odborné aktivity Ústavu medicínskej etiky a bioetiky, spoločného pracoviska Inštitútu pre ďalšie vzdelávanie zdravotníckych pracovníkov (IVZ) a Lekárskej fakulty Univerzity Komenského (LF UK) v Bratislave.

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