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Ethical and Legal Aspects of the Personalised Medicine

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Abstract Personalised medicine is a term that refers to medicine specifically designed to an individual, based on its genomic information. Since sequencing genomes became a fact of life, the concept of individualized healthcare has become a source of great hope. The premise of personalised medicine is that, during the following years, the focus of medical activities shall be moved from the treatment of illnesses to the maintenance of patient's health, through biotechnology. Consequences following personalised medicine are not simple, since it is not isolated phenomenon, but the one followed by the social, political and legal decisions. Legal decisions should relate to the subjective patient's rights, as well as objective medical law: treatment, informed consent, clinical experiments, processing the data, privacy, non-discrimination, etc. Finding the right balance between researchers' needs and subjects' protection is an ongoing regulatory exercise, in which all social actors have to participate by creating a frame for functioning of personalised medicine.

Keywords: • next generation sequencing • human genome • regulatory framework • patients' autonomy • regulatory balance •

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28. POSVETOVANJE MEDICINA, PRAVO IN DRUŽBA
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Etični in pravni vidiki personalizirane medicine

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Povzetek Personalizirana medicina je pojem, ki se nanaša na medicino, zasnovano posebej za pozameznika in temelji na genetskih informacijah. Ker je sekvenciranje genomov postalo dejstvo življenja, je koncept individualiziranega zdravstvenega varstva postal vir velikega upanja. Predpostavka personalizirane medicine je, da se v prihajajočih letih pozornost zdravstvene dejavnosti premakne od zdravljenja bolezni ter se osredotoči na vzdrževanje zdravja bolnikov s pomočjo biotehnologije. Posledice, ki sledijo personalizirani medicini, niso enostavne, saj ne gre za izoliran pojav, temveč jim sledijo družbene, politične in pravne odločitve. Pravne odločitve bi se morale nanašati na subjektivne pravice pacientov kakor tudi na objektivno medicinsko pravo: zdravljenje, informirano privolitev, klinične preizkuse, obdelavo podatkov, zasebnost, nediskriminacijo ipd. Iskanje pravega ravnovesja med potrebami raziskovalcev in zaščito subjektov je stalen nadaljujoč se regulativni postopek, v katerem morajo sodelovati vsi družbeni akterji tako, da ustvarijo okvir za delovanje personalizirane medicine.

Ključne besede: • sekvenciranje naslednje generacije • človeški genom • regulativni okvir • avtonomija bolnikov • regulativno ravnovesje •

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1 Introduction

Personalised or precision medicine is a term that refers to medicine that is specifically designed to a given individual, based on its genomic information. It is the result of the emerged technologies that allow scientists and physicians to build upon patient's characteristics in diagnosing illness (patients family history, social history, medical history, presenting symptoms) (Konski, 2016: 1). In the last years, particularly since sequencing genomes became a fact of life, the concept of individualized healthcare has become a source of great hope (Brothers & Rothstein, 2015: 43). Breakthroughs emerged already in the last fifty to sixty years as discovery of structure of DNA (reported in 1953) and genetic code (in 1966) led to the establishment of the so-called "central dogma" of the molecular biology (DNA makes RNA makes protein). In 1977, Frederick Sanger and the others developed DNA sequencing method.[1] In 1991 the Human Genome Project (hereinafter: HGP) was launched and in 2003 it was finished. The main tasks of the HGP were to read and record the genetic instructions contained within the human genome and provide that information to researchers worldwide freely and without restriction. It also aimed to sequence the genomes of several other organisms important to medical research, such as the mouse, fruit fly and nematode worm. It did this using the most up-to-date DNA sequencing methods available at that time. Since the full human genome sequence became available to the scientific community, progress of research into human health and disease has accelerated dramatically. However, the project was not only about sequencing. It also had a number of other important scientific and social implications. Those were committed to exploring the consequences of genomic research through its Ethical, Legal and Social Implications programme (Human Genomre Project). In the last decade, the genomes of different species have been sequenced – including first human personal genome in 2008 – and the first synthetic genome was produced and used to start up a bacterial cell. Different projects came out from these advances: sequencing of disease genomes, including cancer; development of biobanks, or offering of genetic tests directly to consumers (hereinafter: DTC) (Cordeiro, 2014: 165). Technologies such as next-generation sequencers have become less expensive and more suitable for clinical application, and as a result, personalized medicine has become established in a growing number of clinical areas (Brothers & Rothstein, 2015:

[1] A gene is a descrete sequence of DNA nucleotides, http://www.dnaftb.org/23/bio.html, Last accessed 23.01.2019.; DNA sequencing, https://www.khanacademy.org/science/high-school-biology/hs-molecular-genetics/hs-biotechnology/a/dna-sequencing, Last accessed 23.01.2019.

43). The development of genetic sequencing and the discovery and use of biomarkers has given the clinicians new tools to better diagnose patients and develop more targeted treatments. For example, before the advent of genetic sequencing, a clinical trial of treatment for cancer might have demonstrated a twenty-five percent success rate. However, even with this degree of efficacy, of every four patients treated, only one patient would benefit from medication and the other three would receive no benefit and would also be subject to any adverse side effects of the treatment (Konski, 2016: 1). Today, genetic sequencing might reveal subset of patients with a specific genetic mutation who would be most likely to respond to a particular treatment thereby allowing for a much higher success rate with a particular drug. This benefit is one of the most significant characteristics of personalised medicine – what is commonly referred to as „the right treatment, for the right patient, at the right time" (Konski, 2016: 2). Advances in genetic testing allow diagnosis of diseases, identify risk of genetic transmission of diseases, assess future risk of disease, and help target treatments. Standard of medical researches so far has been that illness is being analysed through sequencing of one gene in one moment. However, personalised medicine promotes, as system medicine approach, possibility of analysing of all genes of individual patient (Brothers & Rothstein, 2015: 43).

The implication of the personalised medicine has expanded in scope and complexity. Social consequences following personalised medicine are not simple, since it is not isolated phenomenon, but the one that should be followed by the social, political and legal decisions. Legal decisions should relate not only to the subjective patients' rights on different levels, but also the objective medical law in all of its aspects: treatment, informed consent, the issue of necessity of medical indication for treatment, clinical experiments and proceedings with examinees, increased amount of health information (and, therefore, processing of data, data privacy, right to information, publishing of data of public interest, non-discrimination, physician-patient relationships and liability), disparities in healthcare (cost and access to healthcare and access to information technologies), etc. (Sjeničić, 2011: 436; Brothers & Rothstein, 2015: 43-44).

2 Increased amount of health information

High amount of data created by using genomic technologies are basis to many predictive, diagnostic and therapeutic applications of personalised medicine. For example, when it comes to biobanks, genetic information has the potential to link biological material to the individual, from which it originated. The information included in biobanks for research purposes is usually linked to other data. Furthermore, respect for private life, in the case of genetic information deserves careful analysis as this information relates not only to the individual, but also to his/her family. Since, in the case of genetic information, privacy rights can blend into the family rights, this should be explained in the clearest terms to biobank donors, which is not an easy task. It is also important to implement safeguards to protect confidentiality agreements in the context of biobanks and to prevent or minimize confidentiality breaches that could considerably damage individual and public trust (Cordeiro, 2014: 167).

Furthermore, the capability to use genomic information in clinics depends on health information technologies, existence of Electronic health record (hereinafter: EHR) and EHR networks, which are available mostly in the highly developed countries. Health information are traditionally in the possession of healthcare providers. By the development of the personalised medicine, responsibility for health is transferred more to patients. This requires also possession of individuals over personal health data, which turns us back to the patients' access to information technologies (Brothers & Rothstein, 2015: 45).

Transferring health data over electronic devices also makes the data specifically vulnerable and open to third parties. These issues open the questions of informed consent to data processing, privacy of data, confidentiality, discrimination on the basis of data, liability for revealing of genetic data, change of physician-patient relationship.

3 Informed consent

Any collection of private data falls under the rules of informed consent obtaining. This is emphasised in the cases of sensitive data, amongst others, health data. Considerable data set related to patients' health is collected, for example, by biobanks. Biobanks are organised collections of biological material and associated information. They can vary in terms of nature, size, aim, duration,

ownership or governance model (Cordeiro, 2014: 165). If informed consent is relevant in all medical issues, in biomedical ethics it is a cornerstone. International and many national legislations require that biological material and associated information are only used for research purposes with the knowledge and consent of the person from which these were derived (Cordeiro, 2014: 166; Law on personal data protection of Serbia, Article 17; Law on human cells and tissues of Serbia, Article 22; Regulation (EU) 2016/23/EC, Article 13). On the other hand, there is considerable debate about whether the traditional informed consent paradigm is appropriate for large-scale research projects such as biobanks, or which is the adequate type of the informed consent for this purpose. Different authors present different arguments to sustain that the classical models of informed consent are not adequate to genetic biobanks and should be adapted or substituted by different paradigms (Cordeiro, 2014: 166). These arguments are: a) the scope of the original consent regarding secondary uses of samples and the impracticality of the constant need for re-consent; b) the complex issue of authorization or request for sample destruction; c) the nature of the information to provide to donors; d) the difficulties in fully guaranteeing genetic sample anonymity; and e) the lack of clear and uniform rules to delimit the extent of property rights over samples and research results (Cordeiro, 2014: 166). Other authors propose that informed consent models should be avoided (Kettis-Lindblad, 2006: 433-440). Alternatively, it should be assumed that participants are willing to delegate decisions on proxies, which most of the times are research ethics committees that are better placed to evaluate and manage the situation. Some authors suggest adopting undetermined models such as broad or open consent (Lunshof, Chadwick, Vorhaus & Curch, 2008, according to Cordeiro, 2014: 166). Obviously the clear rules, essential in this field, are lacking. In searching such rules, one must have in mind that they have to reflect principles of liberty of researches, protect common good and human right to enjoy benefits of science, on one side, and to reflect autonomy of research subjects, i.e. human right of personal autonomy, on the other.

The other disputable issue related to the informed consent is testing of the most vulnerable population which is, sometimes, incapable of consenting. Such consent should be given by legal representatives only after being provided with sufficient information. Beside, whenever possible, the will of the person being tested should be considered in proportion to his/her degree of maturity and capacity to understand (Cordeiro, 2014: 168). This is the attitude is accepted in

many national legislations, in general, and not only related to genetic testing (Oviedo Convention, Article 6; Law on patients' rights of Serbia, Articles 19 and 25; Law on patients' rights of Slovenia, Articles 26, 33 and 35; CRPD, Article 12).

Since genetic information may reveal both personal and familial health or ancestry information, issues of consent and privacy are paramount in genetic studies and tests used in personalised medicine. The ability to obtain consent to future undefined research is central to personalised medicine development. Need to re-examine tissue samples for a different research outcome than originally described often arises. Re-consent of tissue donors for a different research objective may be neither feasible nor possible, and it is unclear whether it is required in all circumstances (Knowles, Luth & Bubela, 2017: 487-488). On the other hand, the autonomy of data subject and personal information must be protected, as much as it is possible in the given circumstances. Furthermore, a laboratories expand analysis and look beyond single genes, the issue of incidental findings gain importance. Should patients be informed about findings in genome regions that differ from the focus of the original search? And what if the search is conducted without seeking the patients' consent? According to relevant legal norms, patients have a right to decide what to be and not to be tested for. Furthermore, they also have a right to know and a right not to know (Cordeiro, 2014, 168; Damm, 2011: 14,15; Sjeničić, 2011: 436). This right relates to the own genetic constitution, but also to the imposed information (Damm, 2011: 15).

Personalised medicine developers complain that the balance of regulations often emphasize individual autonomy and control over personal health information rather than the research enterprise and creation of a research platform of genetic information and resources, creating a barrier to personalised medicine development. Finding the right balance between researcher needs and subjects' protection is an ongoing regulatory exercise. Therefore, all social actors, science, political and legal decision-makers, have to participate in creation of the frame of functioning of personalised medicine, since it really exists in the wide interdisciplinary milieu. This should be ongoing activity, since personalised medicine is continuously surprising us with the new discoveries.

4 Privacy and confidentiality issues

Privacy is a condition of limited access to an individual or information regarding an individual (Brothers & Rothstein, 2015: 45). Privacy violation represents entering the intimacy of the individual against his will, and disclosure of his data (Đukić, 2017: 50). Confidentiality is a condition under which information obtained or disclosed within a confidential relationship is not re-disclosed without the permission of the individual. Security refers to the physical and electronic measures granting access to personal health information to persons or entities authorized to receive it and denying access to the others (Brothers & Rothstein, 2015: 45). Privacy i.e. health data protection is relevant for several reasons: possible stigmatisation or discrimination if sensitive information is inappropriately disclosed; due to stigmatisation and embarrassment patients may withhold relevant information from their health practitioners, and thus compromise the treatment; if out of fear from stigma and embarrassment infectious patients withhold the relevant information from their practitioners, this can jeopardise public health interests (Brothers & Rothstein, 2015: 45). Development of EHR or EHR networks increases the risk of privacy violation, since EHRs are comprehensive (containing most relevant minimal data set from all patients' health records), longitudinal (containing health records over an extended period of time) and could be transferred at one moment to multiple parties (Brothers & Rothstein, 2015: 45). Proposals for resolving of this problem is to give to patients' control over their EHRs, to limit third-party access to these data, and to introduce data segmentation. None of these proposals is fully implementable since many patients are still health and electronic illiterate, healthcare practitioners cannot have incomplete access to patient information, and data segmentation has not yet been adopted to significant extent (Brothers & Rothstein, 2015: 45).

5 Discrimination

Discrimination is making a positive or negative difference between individuals. It is legally or socially unacceptable distinction among individuals. When it comes to health, it is acceptable and necessary to treat individuals differently according to their risk, as long as there is a sound basis to do so. The possibility of genotype-based discrimination was one of the first concerns of scholars examining the ethical, legal and social implications of HGP (Damm, 2011: 11, 17; Deutcher

Ethikart, 2009: 22; Deutscher Bundestag, 2011: 148). An assumption of many genetics researches and public officials was that individuals would be reluctant to undergo genetic testing, despite the clinical appropriateness of doing so, if it could result in discrimination in employment, insurance, mortgages or other important activities (Brothers & Rothstein, 2015: 45). Genomic information could indicate not only that an individual is more likely to develop certain illness in the future, but also that the individual would not be responsive to standard medications and therefore represents an increased morbidity and mortality risk (Brothers & Rothstein, 2015: 45). But, then again, if the health insurance is based on the principle of spreading risk across all individuals with insurance, genetic information should not influence the rise of the premiums. Legislation attempting to prevent genetic discrimination in life insurance and other transactions has been enacted in many countries (German Gendiagnostikgesetz – GenDG, Parts IV and V, 2010; The Health Insurance Portability and Accountability Act, USA, 2013). Most of these laws attempt to prevent genetic discrimination by limiting the information that can be used to assess an individual's likely future health (Brothers & Rothstein, 2015: 45).

6 Access of patients to information technologies

Information technologies should allow patients access to their own health records, which is the vision of personalised medicine. This should be realised primarily through existence of EHR, as minimal patients' data set, collected from patients' records of different health providers where patient has been treated (Sjeničić, 2008: 335-337). The centrality of technologies makes a lot for empowering of patients to monitor their own health and makes positive health behaviour changes. Personalized medicine reflects general trends in healthcare to encourage patients to use information technologies in order to overtake responsibility for their own health needs (Brothers & Rothstein, 2015: 48).

However, on one side, challenge of patients' access to EHR is the information overload, having in mind that he is usually the medical lay person. On the other side, patient can benefit from an electronic health portal if he has the access to internet services and an internet-capable device, as well as if he has necessary computer literacy. These are usually the patients which are already well served by the healthcare system, and rarely the members of the vulnerable groups which are anyway lacking health services due to their vulnerability and inability to reach

the health system: persons with disabilities, elderly people, socially vulnerable, etc.

7 Cost of accessing to personalised medicine

Laboratory tests, such as next-generations sequencing are likely to be costly. Ten years ago, they were offered at price of 1000 USD (Pollack, 2010). Today, they are, for example, offered at price of 99 USD for ancestry information, and at price of 199 USD for ancestry and health information (23andMe). Patients with no insurance, as well as patients with insurance designed to provide only urgent care, are unlikely to benefit from these advances. National health insurance systems generally limit coverage to treatments with established efficacy. They are usually slow in adopting personalized medicine approaches, and thus they might be, for some time, available only for private market (Brothers & Rothstein, 2015: 47). Also, patients from developed countries will receive benefits from personalized medicine rather then, those from developing countries. Medical problems that cause the most morbidity and mortality in developing nations are comparatively rare in the developed world. If personalized medicine is to be efficacious for patients from developing countries, then research efforts focused on personalized medicine will need to expand to include work on the medical conditions endemic to these areas (Brothers & Rothstein, 2015: 48), and that induces some costs.

8 Validity and utility of results of DTC

Genetic tests can be performed at different stages – preconception, preimplantation (on human embryos), prenatal (on a fetus), on newborns, during childhood and adulthood. Different technologies can be used and serve different purposes – diagnostic, predictive of disease or response to drugs, forensic or research. However, as testing human genes and genomes can constitute a profitable marketable activity, gene tests are currently offered not only by public laboratories, but also by private companies, all at competitive prices. They market the tests for our individual responses to particular drugs and chemicals, our ancestry details, genetic matchmaking, our predisposition to develop different conditions in the future or our genetic diseases. All this is promised as such so long as we agree to provide a sample of our DNA for analysis, which is possible by providing a blood or saliva sample. Challenges that exist here and that are

posed by the expanding of tests to DTC genetic tests are mostly related to validity of the test results. Tests are mostly offered via internet, television or other media, without involvement of an healthcare provider, practitioner or genetic counselor. Consumers are then unprotected from damaging effects that may arise from misleading or unhelpful information (Cordeiro, 2014: 167).

Consumers are interested in three levels of quality of genetic testing results: analytical validity, clinical validity and clinical utility. Analytical validity, measure of tests' detection accuracy, must be well established and certified, which requires that countries license laboratories that perform genetic testing by requiring specific professional training, clear record keeping standards, and periodical assessment methodologies, quality control norms introduced, as for clinical laboratory or pregnancy tests (Cordeiro, 2014: 167).

Translating positive result into clinical significance, which determines the clinical validity of the test is not straight-forward and involves mastering accurate scientific notions of probability, risk and variance. Test's results and limitations should be explained and understood as clearly as possible.

And at the end, tests clinical utility, or the usefulness of the test's results in terms of prevention, diagnosis or treatment is hard to estimate, particularly when no therapy or prophylactic measures are available. Therefore, decision to undertake genetic testing should be preceded by comprehensive informed consent process that includes what the test can and what cannot predict and the existence or inexistence of targeted therapeutic or preventive strategies (Cordeiro, 2014: 167-168).

By 2008, *Navigenics*[2] successfully applied to have its test licensed in New York, and also put aside marketing to consumers, aiming instead at doctors. It also aimed corporations that could use the test as part of their employee wellness programs. Since then *Navigenics* offered only health-related information, not genealogical data, as *23andMe*'s does (Pollack, 2010). Actually, in June 2008, California health regulators sent cease-and-desist letters to *Navigenics* and 12 other genetic testing firms, including *23andMe*. The state regulators asked the companies to prove a physician was involved in the ordering of each test and

[2] In July 2012, Navigenics was acquired by Life Technologies, [3] which was acquired by Thermo Fisher Scientific in February, 2014., https://en.wikipedia.org/wiki/Navigenics, 23.01.2019.

that state clinical laboratory licensing requirements were being fulfilled. In August 2008, Navigenics and 23andMe received state licenses allowing the companies to continue to do business in California.[3] This process demonstrates that public health authorities play a key role in demanding the necessary safety and quality standards for genetic tests in order to protect consumers (Cordeiro, 2014: 168). Food and Drug Administration (hereinafter: FDA) has had a hard time to put in adequate legal framework Next Generation Sequencing (hereinafter: NGS) tests which fundamentally differ from traditional diagnostic tests by the volume of data they generate, the lack of *a priori* intended use, and the unlimited number of clinical interpretations possible from a single sample. These fundamental differences did not fit within FDA's regulatory framework for traditional diagnostic tests (Kwon, 2016: 955). FDA made efforts to modernise its regulatory approach to accommodate personalized medicine. In 2013, first NGS test was approved. However, since NGS tests are rapidly evolving, FDA is exploring ways to further modernize its regulatory framework (Kwon, 2016: 958). Namely, it is important to ensure public confidence in the tests, but premature surveillance and un-flexible regulatory framework may lead to „absurd" results, and stop development of personalised medicine (Kwon, 2016: 960).

9 Provider-patient relationship

The interpretation of the whole-genome sequencing results, formulating prevention and treatment strategies based on genomic information and applying pharmacogenomics principles and products, require adequate training of physicians to provide essential services of personalised medicine. Beside the lack of training in this context, there is also a lack of time needed for number of clinical tests, pretest genetic counselling, interpretation of the information and applying the genomic insights in designing a treatment plan (Brothers & Rothstein, 2015: 46). The solution to this problem could be that nurses or other alied healthcare providers are given training and greater responsibility in counselling or follow-up or that the patients are given and assumed to have larger role in their health management. Still, all these solutions bring to the change of the physician-patient relationship (Brothers & Rothstein, 2015: 46).

[3] https://en.wikipedia.org/wiki/Navigenics, 23.01.2019.

With the development of medical technologies, the complexity of medical interventions increases, which brings to increased risk from the error. The parties that can be sued are: manufacturers of genome sequencers, testing laboratories, pharmaceutical companies, medical device manufacturers, pharmacists and hospitals and physicians who are responsible for a patient's overall diagnosis and treatment. This brings to change in the provider-patient relationship and the level of confidence patients have in physicians (mostly in negative direction) and patients have in medicine possibilities (mostly in positive direction).

10 Intellectual property rights

Last, but not least, it is important to mention disputes about intellectual property rights on genes and ownership of genetic information. One such issue, which implicates both the law and ethics, is: what does it mean to "own" a gene, and who is the owner? This may seem like an intellectual abstraction, but the answer is of great practical importance to medicine and research (Knowles, 2017: 1).

Patent is a property right issued by a government to one or more inventors, which allows the patent holder to prevent others from making, using, importing, offering for sale or selling the patented technology. However, not every discovery is patentable; only discoveries that meet the criteria of novelty, non-obviousness and utility can be protected by a patent (Konski, 2017: 3; Andrews, 2002: 803). The usefulness of the inventions must be specific, substantive and „credible". The patent application must also be adequately „enabling", i.e. it must describe the invention fully, in a way that would allow another person who is skilled in that field to reproduce the invention. This requirement is particularly important because one of the purposes of patent law is to ensure that the public gets information in exchange for the monopoly granted to the patent holder. Other inventors can use that information to further their own research, but cannot make or use the patented invention itself without the permission of the patent holder (Andrews, 2002: 803).

Based on the discussion in theory, and the disputes in front of the courts, genes are somewhere in between patentable and unpatentable substances. Laws do not allow patents on products of nature because the public would not be gaining anything new. This relates to genes and scientific formulas (Andrews, 2002: 804). Patenting the genes has a great negative impacts on diagnosis and treatment. Since patent holder has the right to control any use of "their" gene 20 years from

the date that a gene patent was filed, they can prevent a doctor from testing a patients' blood for a specific genetic mutation, and can stop anyone from doing research to improve a genetic test or to develop a gene therapy based on that gene. That has happened with Athena Neurosciences Inc., which holds the patent on a gene that is associated with Alzheimer disease. No laboratory, except theirs, can screen mutations in that gene. It also happened in 2001 with US Myriad Genetics which was granted a European patent related to BRCA 1 breast-cancer-associated gene. The patent covers all methods for diagnosing breast cancer by comparing a patients' BRCA 1 gene with the BRCA 1 gene sequence that Myriad describes in its patent. This company requires that all the samples be sent to its laboratory. However, French physicians are concerned that Myriad's test only assesses 10 to 20% of potential BRCA 1 mutations, and this is proved on one family where the test has missed (Adrews, 2002: 804). The problem is that various mutations in the same gene can cause a particular disease. When companies possess the patent, do not let anyone else screen the gene sequence that they have patented for other mutations, it lessens the chance of other disease-associated mutations being found (Adrews, 2002: 804).

Gene patents also hamper pharmacogenomic research. Many drugs work on only a percentage of patients who use them. Genetic testing can help distinguish those patients for whom a drug will work from those for whom it will not. Also, research to find additional genes that are responsible for diseases is also impeded by the gene patents. Besides, gene patents also undermine the scientific method. Researchers who discover and patent genes have financial incentives fo promote the use of those genes for diagnostics, sometimes before sufficient data are available to assess how well a test predict future disease (Adrews, 2002: 804).

On the other side, to regard genetic information as personal property may resolve many of the worries associated with uninhibited genetic research, but popular attitudes towards DNA may harden or change over time, as the public becomes more familiar with genetics (Knowles, 2017: 2).

Besides, US patent office, for example, holds that a human gene as it occurs in nature, cannot be patented, but, if a DNA sequence is purified and isolated in the form of cDNA[4] or is part of a recombinant molecule or vector, then this

[4] cDNA is a combination of cloned cDNA (complementary DNA) fragments inserted into a collection of host cells, which together constitute some portion of the transcriptomeof the

"invention" is patentable under the precedent of the previous "adrenaline case". Namely, the 1912 case of *Parke-Davis versus H. K. Mulford (Parke-Davis v. H. K. Mulford*, 196 F. 496) upheld a patent on adrenaline, a natural hormone that was found in animal glands. The patent applicant identified, isolated and purified the active ingredient — adrenaline. This created a product that did not exist in nature in that precise form and that could be used for medical treatment. The US patent office holds that a human gene as it occurs in nature cannot be patented (Adrews, 2002: 804).

The issue of ownership of genetic information was raised, for example, at Myriad, which has collected a large amount of genetic and health information from test it has offered. These information, could provide insight for new genetic tests and on genetic variants linked to diseases other than those focused on in Myriad's test. USA Health Insurance Portability and Accountability Act, mostly known for its protections on patients' privacy, also includes provisions guaranteeing patients access to their health information. Several patients have filed a complaint to gain access to genetic information beyond what is contained in the report of their test results. The patients sought after full access to the genetic information for the purpose to proactively monitor their own cancer risk and be able to share their data with other research groups. After initially refusing to provide the data to the patients, Myriad reversed course and provided the clients with additional information. Nevertheless, American Civil Liberties Union which represented the patients, reported that the group of patients wants an official decision supporting patients' right to their genetic information. That would ensure that Myriad turn over the full genomic record to all patients who request their records in the future (Leah, 2016: 1-2).

11 Conclusion

Personalised medicine promises to provide „the right treatment, for the right patient, at the right time". The social challenges, that should be resolved before going further with the advances, or, at least, parallel to them, are not simple, since personalised medicine is not an isolated phenomenon, but the one existent in the wide interdisciplinary milieu. Legal decisions should relate not only to the subjective patients' rights on the different levels, but also the objective medical

organism and are stored as a "library", https://en.wikipedia.org/wiki/CDNA_library, Last accessed 19.01.2019.

law in all of its aspects: treatment, informing/genetic counselling, obtaining the consent, processing the data, data privacy, publishing of data of public interest, etc. Therefore, all social actors, science, regulatory bodies on the market, courts, political and legal decision-makers, have to participate in creation of the frame of functioning of personalised medicine. Of course, the complexity of the personalised medicine phenomenon should not serve as an excuse for an inaction. Action should be focused on finding balanced solutions which would allow the further development of the personalised medicine in benefit of public and individual health, and, at the same time, protect existing human rights and values, such as patients' autonomy, privacy, confidentiality, right to information and right not to be informed, and other personal rights.

Legislation, cases

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