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LEGAL AND ETHICAL ASPECTS OF THE PARTICIPATION OF PERSONS WITH RESTRICTED ACTIVE LEGAL CAPACITY IN GENOME STUDIES

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Abstract. The goal of the Estonian Genome Project is to establish a database consisting of phenotype and genotype data of the majority of the Estonian population. The database will allow carrying out genetic and health studies in order to identify genes that cause and influence common diseases, prepare new medicines and introduce the methods of preventive health care. The aim of the present article is to discuss the positive and negative sides of the inclusion of persons with restricted active legal capacity in the large-scale population-based gene studies, as well as its medical, legal and ethical aspects. The right of the minors to participate in genome studies on the one hand, and the obligation to protect them from exploitation on the other, still remain a matter of discussion.

Keywords: genome study, Estonian Genome Project, restricted active legal capacity

1. Introduction

The goal of the Estonian Genome Project is to establish a database (the Gene Bank) consisting of phenotype and genotype data of the majority of the Estonian population (1.4 million inhabitants). On the basis of the data stored in the Gene Bank it will be possible to acquire new knowledge concerning the cause and pathogenesis of common diseases. At different periods of the elaboration of the Estonian Genome Project there have been different topics of ethical debates, the engagement of people with restricted active legal capacity as well as the lowest age limit of persons participating in the Project among them.

According to the General Part of the Civil Code Act of the Republic of Estonia (2002), persons who have attained 18 years of age (adults) have full active legal capacity. Persons who are under 18 years of age (minors) and persons who due to mental illness, mental disability or other mental disorder are permanently unable

to understand or direct their actions have restricted active legal capacity. The legal representatives of a person under 18 years of age are his or her parents; the legal representative of a person with restricted active legal capacity is his or her guardian. It should be mentioned that pursuant to the Estonian Act on Human Genes Research (2001), the consent of legal representative does not suffice, if the person him- or herself is opposed to providing a tissue sample or to the collection of descriptions of his or her state of health.

The present article will discuss the positive and negative sides of including the persons with restricted active legal capacity (incl. children) in the large scale population-based gene studies, as well as its medical, juridical and ethical aspects.

2. Medical aspects

The possible advantages and disadvantages of genome studies

First, it should be stressed that at the present day genome projects are research projects without direct therapeutic element. Relying on their results it could be possible in the future to introduce the principles of preventive medicine. So far, the discussions have been mostly centred on predictive testing which is usually conducted to ascertain the monogenic disease that has appeared in the family. Population-based study is focussed on identifying the genes that are responsible for diseases prevalent in the society (polygenic and multifactor diseases), could be avoided with prophylaxis (proper way of living) and can be treated. So far, the only possible advantages and disadvantages for genetic research have been cleared up and reported for predictive testing and, though not always, they could be indirectly relevant also in the case of genome studies. The possible advantages of predictive testing that have been proposed are: 1) uncertainty about having the disease can be minimised; 2) anxiety about possible early signs of the disorder can be relieved; 3) it can eliminate the need for more expensive and less accurate tests in the future; 4) more accurate genetic counselling becomes possible, also children who might benefit from genetic counselling in the future will be identified; 5) family uncertainty about the future can be reduced; 6) planning for the future and a more suitable lifestyle, education and career can be more practical; 7) the person's expectations for the future can be more realistic; and 8) it is easier to accept a person's carrier status and incorporate into his or her identity; and 9) the person's attitude towards reproduction will be more responsible (Working party of the Clinical Genetics Society 1994:785–797; American Society of Human Genetics 1995:1233–1241, Chan 2001:50–52, Paulson 2002:627–646). The potential psycho-social risks testing, especially in childhood, includes 1) the child's right to decide whether or not to be tested in adulthood will be removed; 2) the possibility to damage the child's sense of self-esteem and get stigmatised associated with genetic abnormality, even in the absence of phenotypic abnormality; 3) the potential for inhibiting parent-child bonding; 4) disruption of normal family relationships because of guilt on the part of parents or on behalf of the unaffected siblings (so-called

survivor guilt); 5) the potential for a variation of the "vulnerable child syndrome"; 6) modification of parental expectations (often subconsciously), also parents may start to treat their child as diseased/disabled (genetic discrimination); 7) possible future difficulties in obtaining a job and life insurance (Working Party of the Clinical Genetics Society 1994:785–797, American Society of Human Genetics 1995:1233–1241, Chan, 2001:50–52).

Whereas single-gene disorders are rare, conditions caused by an interaction between genes and environmental factors are frequent and include disorders such as cardiovascular diseases, several cancers, asthma, diabetes, mental disorders etc. Preventive aspects of work in medical genetics include identification of high-risk individuals with respect to common disorders for the purpose of preventing disease (e.g., heart disease) or securing early diagnosis and treatment (different forms of cancer). At present there are significant research efforts aimed at developing somatic cell gene therapies or therapies to improve or block the function of genes (Friedman Ross and Moon 2000:873–879). Also, predictive medicine enables to identify healthy individuals who are either susceptible or resistant so that primary-prevention efforts (e.g., diet, lifestyle and exercise) or secondary-prevention efforts (early detection or pharmacological intervention) can be initiated if needed.

The aims of the large-scale population-based gene studies also include the detection of the causes of several diseases, working out appropriate medicines and the application of the methods of preventive health care in the future.

3. Legal aspects

Background of the Human Genes Research Act (HGRA)

No international organisation with which Estonia has been joined requires that kind of law but it was important to regulate the main principles concerning the large-scale population-based genetic studies on legal basis considering the developmental directions in the future.

The Constitution of the Republic of Estonia recognises the right to carry out scientific research, not expressly regulating biomedical research but protecting anyone from medical or scientific experiments that are conducted against one's free will. In addition to that, the Constitution recognises the principle of legitimate expectations. The Convention on Human Rights and Biomedicine (1997) and the Universal Declaration on the Human Genome and Human Rights (1997) belong among the most important international documents of the biomedical field. Although these documents can be considered only as "soft laws", they set forth the main principles, i.e. the requirement of informed consent; the right to know and the right not to know the results; the evaluation and acceptance of ethics committees; confidentiality and non-discrimination, etc. The Republic of Estonia ratified the Convention in 2002. The HGRA (2001) was prepared under the guidance of the Estonian Ministry of Social Affairs and the Estonian Parliament approved it in

December 2000 (Nõmper 2002:99–104). The main above-mentioned principles of the international acts are implemented in the HGRA.

The creation of Gene Bank

The creation of a gene databank for research purposes is governed by two main principles. First, its creation is based on the idea that the human genome is a national resource, echoing the recognition enshrined in the 1997 UNESCO Universal Declaration on Human Genome and Human Rights that the human genome is "the heritage of humanity". Second, it is governed by the idea of "genetic altruism". The latter is hoped to encourage a wide population participation motivated by the contribution to the improvement of diagnostic and therapeutic medicine brought about by the storage and processing of genetic material. The entity that is positioned between the donors and research/business community is the Gene Bank, entrusted with the collection, storage and processing of the material, and funded by the Estonian State (European Commission 2003:73–75).

4. Principles of the Human Gene Research Act

The requirement of informed consent

One of the key principles of the Act is the requirement of informed consent. Unlike the Icelandic Health Sector Database, the Estonian Gene Bank is founded on expressed consent. In order to be able to collect data about a person, the chief processor of the databank must receive a free informed consent from that particular person before (Nõmper 2002:99–104).

At the same time, the Act does not establish the lowest age limit for a gene donor. The missing requirements on age result indirectly in the requirements concerning the consent of the gene donor.

Validity of consent of the gene donor

However, in order to protect the gene donors' rights, such consent is deemed valid only if the following conditions are met: 1) the gene donor and his or her legal representative or guardian have been given all the relevant information as set forth in the Act; 2) the legal representative or guardian has expressed the consent freely; 3) the gene donor himself or herself has not opposed to providing a tissue sample or the collection of descriptions of his or her state of health (Nõmper 2002:99–104). Furthermore, the Act provides that persons who are unable to understand the content and meaning of consent cannot be gene donors. Subsection 9 of the Act prescribes the voluntary nature of gene donation, i.e. the conscious and voluntary consent of the gene donor as a presupposition to the gene study.

The consent of persons with restricted active legal capacity

The regulation no 125 (2001) dated on 17 December 2001, by the Minister of Social Affairs of the Republic of Estonia establishes the form of consent to become a gene donor, its execution and preservation. According to this regulation, the authorised processor of Gene Bank has to be convinced while introducing and filling the form of the consent that the person is able to understand its content and meaning. For comparison, according to the article 5 of the Convention on Human Rights and Biomedicine (1997), the intervention in the health field may only be carried out after the person concerned has given free and informed consent to it. This person shall beforehand be given appropriate information as to the purpose and nature of the intervention as well as on its consequences and risks. The above-mentioned article is not limited only to adults, which means that the minors should be informed as well. According to clause 2 of the article 6, if a minor according to law does not have the capacity to consent to an intervention, the intervention 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. When compared to the sub-section 13 of the HGRA (2001), the last one is stricter in this regard as the understanding and will of the parent or guardian is not considered to be sufficient – regardless of their consent, the gene donor must not be opposed to the intervention like mentioned in the article 17 of the Convention of Human Rights and Biomedicine (1997), but the gene donor must also understand the content of his or her consent.

The institution of the legal representative

It must be noted that in the course of the preparatory works of the Act the requirements of non-opposition and understanding were introduced as a result of choice between leaving the gene donor absolutely in the discretion of its legal representative on the one, or requiring his full consent on the other margin. It was noted that in commercial or day-to-day practice the institution of the legal representative is necessary and sufficient in order to let the person perform as legal subject. On the other hand, in case of participation in gene bank the intervention into one's privacy would be immediate and taking tissue sample (i.e. blood sample) physically painful, the following research would be continuous and results would have much broader and long-term implications than in ordinary business for which the institution of the legal representative was designed. In case of a child, the special problem to be addressed is that they will grow up and as adults, would maybe take a different position from the one their parents have already made for them. On the other hand, it was also accepted that most of the children and disabled indeed could not fully understand all the purposes of use, risks and rights that follow the participation.

The qualification of the gene donor's consent

Consequently, something that was understood as a compromise, was introduced. First, it was decided that a positive assertion by a minor or a disabled person cannot qualify legally as consent and only a legal representative can perform on their behalf when receiving information and expressing consent. Furthermore, additional negative tests were to be introduced. First, as regards the non-opposition clause, it was expected that one of the practical outcomes of the non-opposition test would be to prevent the very young from participating (no child wants a blood sample to be taken), while older children who are able to follow their own reasoning for becoming gene donors, could also overcome the fear and pain of physical intervention. Second, the understanding-test would also prevent the very young from participating since they are not able to understand what their parents are consenting to – verification of understanding is of course depending on the authorised processors. It must be noted that these tests are not some exhaustive selectors that automatically prevent parents or custodians from taking the "wrong" decision for their children or disabled persons; rather they are to be considered as additional criterions to qualify the gene donor's consent.

Comparison with the Medicinal Products Act

A brief comparison with the Medicinal Products Act (1996) shows that the consent to the participation of a person with restricted active legal capacity in a clinical trial of a medicinal product is given by the legal representative of such person, and for a minor who is 7-18 years old to participate in a trial, the consent of the minor is necessary. The Medicinal Products Act does not prohibit the participation of younger that 7 years old children. Due account must be given to the fact that participation in clinical trial involves immediate risks to one's health whereas the collection of blood samples of the gene donors' is a well-standardised medical procedure.

To conclude, the number of children or disabled who would pass the tests set in the HGRA will very likely be limited. It also seems that the HGRA is more restrictive than the Medicinal Products Act in similar areas. Yet and regardless of those tests, there is another question to be answered: would it still be legally justified to involve children in the gene bank?

5. Child protection

The Estonian Child Protection Act (1993, revised 1998) provides for the internationally recognised rights, freedoms and duties of the child and his or her protection. This Act provides the basis for other legislation of general application of the Republic of Estonia concerning child protection. According to this Act, a child is a human being below the age of 18 years. According to the subsection 8 clause 2 of the General Part of the Civil Code Act (2002), a person below the age

of 18 years has restricted active legal capacity. The restricted active legal capacity of a minor of at least 15 years of age may be extended if this is in the interests of the minor and the level of development of the minor so permits.

The best interests of the child

According to the subsection 3 of the Estonian Child Protection Act (1993, revised 1998), child protection is based on the principle that the best interests of the child shall be a primary consideration at all times and in all cases. In addition one must refer to the United Nations Convention on the Rights of the Child (1989) that states in article 3 that the best interests of the child shall be a primary consideration in all actions concerning children. The same idea is included in article 24 clause 2 of the Charter of Fundamental Rights of the European Union (2000), according to which in all actions relating to children, whether taken by public authorities or private institutions, the child's best interests must be a primary consideration. According to article 2 of the Convention on Human Rights and Biomedicine (1997), the interests and welfare of the human being shall prevail over the sole interest of society or science.

6. Ethical aspects

The competence of child

An adult is able to give informed and binding approval. When speaking of children, the question is whether and how competent they are in their decisions concerning gene donating, not only in granting consent but in later enforcement of their rights.

The consent of child as such is problematic. A child without life experience on decisions and their long-term consequences can pronounce much easily than an adult. A child can just change his or her decision or it can be emotional, having regard to short-term benefits. Although Section 9 the HGRA (2001) also prohibits exercising any kind of coercion or influencing the gene donor, the violations with children cannot be detected or enforced easily and furthermore, the coercion is not necessarily directed or intentional but caused for instance by rules set in the family upon one's behaviour (for instance "if I behave well at the doctor, mother will give me a candy").

How well can a child understand the kind of specific definitions as "gene", "tissue sample", "gene donation" etc. and recognise their meaning? Are children capable of understanding the reasons why they are gene donors, do they realise what shall be done with the tissue samples taken from them, and what is the benefit of their being gene donors to them or to the society?

The enforcement of rights

To mention the enforcement of gene donor's rights, it must be noted that there is no legal practice today even concerning adults. A conservative approach would require a careful consideration how children would exercise their rights to know and not to know, how they would require destruction of the connection or relation between their personal data and the material collected, etc. The HGRA (2001) establishes the gene donors' right to know or not to know their genetic data, to be consulted by specialists in medical genetics and the right to submit additional information about them to the chief processor. In case of children the kind of right to know or not to know and to submit additional information is problematic because obviously the data stored is not that simple in its substance that a child could understand it.

7. Age of the child and his or her maturity

The large-scale population-based gene studies in children raise several questions, particularly with respect to consent and confidentiality. The basic problem is the age of legal majority. Protection of minors can take place in two different ways: either the law states that the opinion of the minor shall be taken into consideration or the parents are presumed to be best suited to make decisions for their children (Friedman Ross and Moon 2000:873–879, Twomey 2002:557–566).

The general legal order supports the idea that children's ability to understand the information and pronounce decisions of legal liability depends on their age and level of development. The age when the children are able to estimate the hidden purposes of their actions is different, but it is possible to draw some general conclusions.

A child below the age of seven years has not usually reached the kind of level of thinking to pass altruistic decisions. But children over the age of seven years can very well understand that participating in some kind of scientific program they will help doctors to cure other children (Mason and McCall Smith 1996:163–165).

According to article 12 of the United Nations Convention on the Rights of the Child (1989), the child who is capable of forming his or her own views has the right to express those views freely in all matters affecting him or her and the views of the child must be given due weight in accordance with the age and maturity of the child. Here, the child's views should be estimated in accordance with his or her age and maturity.

The same idea is issued in clause 1 of article 24 of the Charter of Fundamental Rights of the European Union (2000), according to which children may express their views freely and their views shall be taken into consideration on matters that concern them in accordance with their age and maturity.

An intellectual age for medical and research decisions

It is to be noted that, for instance, the Netherlands lowered the age of majority for medical decisions from 18 to 16 years of age. This was done exclusively for those cases where the sole interest of the minor is at stake. If the patient is a minor over 12 years of age, but not yet 16, the consent of the parents is also required (Wijnberg 2000:105–110). The major international and national guidelines are in agreement that, at least in many cases, a paediatric patient must also agree to participate in the research before it can be performed. To quote the Declaration of Helsinki: "Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian" (1964). Similar provisions about obtaining paediatric consent (which has come to be called the child's assent) are built into the HHS (Department of Health and Human Services) regulations in the United States (Brody 1998:Appendix 3.1) and various British guidelines (Brody 1998:Appendix 4.1, Brody 1998:Appendix 4.2). Obviously, paediatric assent cannot be required if the child is very young. The 1995 report from the American Academy of Paediatrics suggested an intellectual age of seven years (American Academy of Paediatrics 1995a:286–294). The age of seven was also adopted in the 1993 Canadian report (National Council on Bioethics in Human Research 1993). The British Paediatric Association required getting assent from school-age children (Foster 1994:13).

Concrete concepts of health-related procedures are developing by age seven years, a full understanding of the nature and consequences of agreeing to or refusing medical management does not occur until early adolescence, and maybe later (Canadian Paediatric Society 2003:42–45). The experience of being tested and receiving the results can be tolerated well by children if proper support by parents and professionals is available (Twomey 2002:557–566). The Canadian 1993 report (National Council on Bioethics in Human Research, 1993) specifies the age of fourteen as the approximate age of maturity, and it makes clear that although parental involvement is encouraged, the consent of the subject over fourteen is sufficient at least for therapeutic research (Great Britain Advisory Committee on Genetic Testing 1999:21–24, Nelson et al. 2001:1451–1455, Canadian Paediatric Society 2003:42–45).

In the Declaration of Helsinki of the World Medical Association (1964), it is stressed that for a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorised representative in accordance with applicable law. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorised representative.

The British Paediatric Association and the Medical Research Council share the same point of view. They think that non-therapeutic scientific studies in children

can be justified if other children will benefit from them (Mason and McCall Smith 1996:163–165).

The child's freedom in making decisions

According to the clause 1 of the article 24 of the United Nations Convention on the Rights of the Child (1989), States Parties recognise the right of the child to the enjoyment of the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health. States Parties shall strive to ensure that no child is deprived of his or her right of access to such health care services. In the same article, it is stressed that it is essential to develop preventive health care. Article 13 of the Convention on the Rights of the Child establishes that the child shall have the right to freedom of expression; this right shall include freedom to seek, receive and impart information and ideas of all kinds, regardless of frontiers, either orally, in writing or in print, in the form of art, or through any other media of the child's choice. The child has the right and shall be accorded the opportunity to seek, receive and impart diverse humanistic information and to engage in organisations and movements. The child's freedom of expression is not linked to his or her age.

According to the Estonian Child Protection Act (1993, revised 1998), the child has the right to freedom of thought, conscience, religion and expression. Every child has the right to have his or her opinion and the right to express it freely. Every child has the right to be heard out in things concerning him or her at school, at home as well as in administrative agencies.

The role of parents

When we give parents an absolute freedom to make decisions for their children, we would invade the children's rights mentioned above. The limitation and suppression of these rights can appear to be a real obstacle to the development of the child. If we are guided by the opinion that the parents' consent will substitute the one of the child, we presume that, as a rule, parents pass decisions in the interests of their children. A parent's consent can be dealt here as a substitute to the child's decision. It means to say out what the child would have expressed by him- or herself if he or she had been capable of doing so. One can be guided by this theory only in case of small children (child being below the age of three years) who are not able to express their will.

8. Giving people with restricted active legal capacity a chance to participate in the genome project

The main idea of the HGRA is to give people a chance to participate in the genome project but no one is obligated to do it. In essence, it means that parents or

guardians, while giving their consent, cannot obligate anybody to participate in a gene study. It cannot be contended that a person's interests are on the foremost position when his or her participation in a gene study is tied to his or her parents' or guardians' consent.

Possibilities to withdraw

According to the subsection 12 of the HGRA (2001), a gene donor has the right to withdraw his or her consent until his or her tissue sample or the description of his or her state of health becomes coded. After the coding the gene donor has the right to demand the destruction of the data enabling decoding. That means after destruction it is not possible to link the person with the blood sample and health data and the gene studies are carried on with anonymous data without identifying the person. In case the gene donor is revealed illegally, the gene donor has the right to insist all his or her health data and tissue samples collected and stored in the Gene Bank to be destroyed.

9. Problems concerning participation in genome studies

When bearing in mind the prospective possibilities, the database of the genome project as a population-based study should cover the majority of the population. The chance to participate is established by law. The child's participation in the genome project raises the question about a situation that appears when a child becomes an adult and will find that his or her participation has been decided against his or her will. Will it then be the fault of parents for having given their consent, or of the medical staff for carrying out medical procedures? When including children in the genome project, there is definitely a risk that a child will not understand the meaning of his or her consent and its consequences. In ethical, social and legal sense, it seems widely accepted that childhood is a period where the child's values, views and sense of responsibility are in constant development, they cannot be deemed as "completed" or "binding" and thus any non-necessary burdens by taking irrevocable decisions must be avoided? One must also make a reference to J. K. Mason and R. A. McCall Smith (1996) who note that non-therapeutic research with children can be justified only if children can benefit from it, i.e. when a child as a research object cannot be substituted with an adult. The same idea is issued in clauses 1 and 2 of article 17 of the Convention of Human Rights and Biomedicine (1997) treating the protection of persons not able to consent to research, according to which research on a person without the capacity to consent may be undertaken only if the results of the research have the potential to produce real and direct benefit to his or her health; research of comparable effectiveness cannot be carried out on individuals capable of giving consent; the research has the aim of contributing, through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the

ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition; and the research entails only minimal risk and minimal burden for the individual concerned. In the case of persons with restricted active legal capacity, it is controversial whether these conditions are fulfilled and according to the HGRA (2001) persons who are unable to understand the content and meaning of consent shall not be gene donors (Section 13, clause 2), and partial or conditional consent is not considered to be valid (Section 12, clause 2).

The inclusion of people with restricted legal active capacity in the genome project in Estonia can be legally summarised by following the questions that need to be answered individually in each case. Even if only one of the answers is "no", the inclusion of a person should be considered unlawful or unethical.

1. Has the person received the information prescribed in the subsection 12 of the HGRA concerning gene donation, including the rights and risks of a gene donor?

2. Has the person understood the information?

3. Is it beyond reasonable doubt that the parent or guardian is not influencing the person to become a gene donor (incl. allurements, orders, promises, etc.)? Has the child's decision to become or not to become a gene donor not been criticised or praised?

4. Is it beyond reasonable doubt that the authorised processor is not influencing the person to become a gene donor (incl. allurements, orders, promises, etc.)?

5. Has the person had a chance to ask about becoming a gene donor?

6. Has the person had an opportunity to express his or her opinion about becoming a gene donor?

7. Is the person not initiating resistance against taking a blood sample from him or her?

8. Is the person not initiating resistance against his or her questioning?

9. Is the person later capable of making decisions concerning his or her rights as a gene donor through his or her parent or guardian?

10. Does the person or do other persons gain clearly defined benefit from the participation in the gene bank?

10. Discussion

Genetic information will be useful if it provides additional information about aetiology diagnosis, or prognosis compared with what is currently available. For many diseases, this is likely to be the case, and it will lead to greater integration of genetic information into clinical practice and public health (Kaprio 2000:1257–1259).

The growth in knowledge of the human genome will bring with it an extension and acceleration of genetic research. The determination of "genetic predisposition"

to polygenic or multifactorial pathologies will increasingly be possible; hand in hand with the identification of genetic predisposition to the action of pathogens present in the home or in the workplace for late onset diseases. The prognoses that may be inferred from genetic investigations are quite different from those offered by other diagnostic tests, as they identify a risk, as opposed to a disease in its early stages. A large psychological and social cost can be associated with the knowledge of such a predisposition (European Commission 2003:73–75).

In the twenty-first century physicians will help their healthy "patients" to remain so and to manage their health capital in the long term. Predictive medicine comes before prevention and physicians will gradually become counsellors. Predictive medicine should eventually change the nature of medical consultation and in the future it would be better to speak of "individual preventive medicine" (Dausset 2001:57–68).

At present, people with restricted active legal capacity have the chance to participate in the genome project if they are not against it and if their legal representative or guardian has given consent. The inclusion of children is not taking place right now but is under discussion. In case of children, the importance of informing and getting an informed consent is being stressed. At the same time, even an adult does not always understand exactly to what he or she is consenting and nobody considers it to be unethical. It is not unlawful either because the law establishes limits to the inclusion of persons with no decision-making powers. In the case of doubt, it is presumed that the person is temporarily unable to understand the content and meaning of consent in case of temporary disturbance of the mental condition or other circumstances (i.e. intoxication), which excluded his ability to estimate rightly the influence of the operation on his or her interests. An adult's little knowledge or weak ability to think is not a sufficient reason. When we consider minority a reason limiting the ability to estimate consequences rightly, it lays an obligation on the investigator to be convinced that the minor has fully understood to what she or he gives consent (according to the law, to what he or she is not against).

Definitely the studying of genomic data of children should be done in accordance with international conventions. But, if we are guided by the fact that gene researches are working with coded data, internationally under the human studies the scientific research of only identifiable human material or medical data is considered.

The term "restricted active legal capacity" is being used in private law, the Estonian HGRA should belong under public law when minors are being discussed and the different age limits have been set with specific laws in exercising different rights, discharging obligations or violating the law (for instance, the right to elect - at the age of 18, the right to be elected to *Riigikogu* – at the age of 21, the age of criminal liability – at the age of 14, compulsory school attendance – at the age of 7 until 17). Active legal capacity means the ability to perform activities independently. In case of the HGRA, it is been guided by the analogy of the law according to which a person has restricted active legal capacity until the age of 18

(according to the former General Part of the Civil Code Act (in force) the restricted active legal capacity was from seven to 18 years of age).

Traditionally in paediatric medicine, parents are presumed to be best suited to make decisions for their children. Various arguments have been made to support parental control over medical decision making for minor children (Friedman Ross and Moon 2000:873–879, Twomey 2002:557–566). Although health care providers have it downplayed, the current attitude is to give greater weight to the child's developing decision-making capacity (American Academy of Pediatrics 1995b:314–317) and future autonomy (Feinberg 1980:124–153). However, parental autonomy is not and should not be absolute. It would probably be wise to rely on parents to make decisions for their children while remaining open to the possibility that the child may have something important to add.

Evaluating parental requests requires finding the appropriate balance between the child's present and future needs and interests with the interests and needs of the families (Friedman Ross and Moon 2000:873–879, Richter and Bacchetta 1998:303–317). The best way to protect the interests of the child is not found in protectionism from theoretical harms, but rather in means for educating all involved in the decision-making process (Twomey 2002:557–566).

When we are guided by receiving a consent in providing health care service, in case of a minor we decide by his or her consent and the parent's or guardian's consent is asked in case when the patient is not capable of considering the pros and cons of a question with whole responsibility. The subsection 766 of the Law of Obligations Act (2002) even provides that if the decision of the legal representative appears to damage the interests of the patient, the provider of health care services shall not comply with the decision. If the minor has a right to decide over her body, i.e. delivery or abortion, which have far more important consequences than being a donor of gene bank, then the inclusion of children to the Genome Project cannot be unethical if all the requirements established by the law have been followed. Unethical and punishable by law is the act of the one who has influenced the gene donor (i.e. relatives).

As mentioned above, in all activities concerning children and in all procedures in connection with them the children's interests should be considered primary. But the level of development of children is different. Sometimes a ten-year-old child can understand things better that an adult and we have no right to forbid him or her to participate when the law allows him or her to do it. Forbidding a minor to participate in a gene study may restrict his or her fundamental rights. When, for instance, there is some genetic disease in the family, they may be very interested in joining the genome project and also have the kind of level of development that they understand everything. Depending on the level of development of a child more attention should be paid to his or her consent, and not to the fact that he or she is not opposing. It does not seem justified, however, to refuse testing to a fully informed, competent adolescent who is requesting it. In many cases, it may be best to defer the decision until the legal age of majority is reached (Great Britain

Advisory Committee on Genetic Testing 1999:21–24, Nelson et al. 2001:1451–1455, Canadian Paediatric Society 2003:42–45).

The preliminary experience of the Estonian Genome Project has shown that many teenagers have an innovative way of thinking and they are interested in participating in the gene study. It should be stressed that there is definitely a need to prepare counselling information suitable to their age and understanding. As in case of the persons with restricted active legal capacity, the investigators have to ensure that the information will not be used against them. The obligation to protect minors on the one hand and their rights and practical help they could receive from their gene studies in the future on the other, are subjects that need further discussion.

11. Conclusions

1. The goal of the Estonian Genome Project is to establish a population-based database enabling to carry out genetic and health studies in order to identify genes that cause and influence common diseases and prepare new medicines.

2. The Genome Project is carried out according to the Estonian Human Genes Research Act, which is in conformity with international declarations and regulations. So far the Human Genes Research Act has been functioning well and there has been no contradictions to practice.

3. The Estonian legislation enables people with restricted active legal capacity to participate in the Genome Project with the approval of their guardian, if they are not opposed to it.

4. In including people with restricted active legal capacity to the genome project, it is essential to provide information in the form understandable to them.

5. As in the case of persons with restricted active legal capacity (e.g. children) the investigators have to ensure that the information will not be used against them.

6. Depending on the condition of the mental health of a person with restricted active legal capacity or the level of development of a child, more attention should be paid to his or her own will.

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References

American Academy of Pediatrics. Committee on drugs. (1995a) "Guidelines for the ethical conduct of studies to evaluate drugs in pediatric populations". *Pediatrics* 95, 2, 286–294.

American Academy of Pediatrics. Committee on Bioethics. (1995b) "Informed consent, parental permission, and assent in pediatric practice". *Pediatrics* 95, 314–317.

American Society of Human Genetics Board of Directors and American College of Medical Genetics Board of Directors. (1995) "ASHG/ACMG report: points to consider: ethical, legal, and psychosocial implications of genetic testing in children and adolescents". *The American Journal of Human Genetics* 57, 1233–1241.

Brody, B. A., ed. (1998) *The ethics of biomedical research*. Oxford: Oxford University Press, Appendix 3.1; Appendix 4.1; Appendix 4.2.

Canadian Paediatric Society (CPS), Bioethics Committee. (2003) "Guidelines for genetic testing of healthy children". *Journal of Paediatrics and Child Health* 8, 1, 42–45.

Chan, N. S. (2001) "Genetic testing". *Trinity Student Medical Journal* 2, 50–52.

Charter of Fundamental Rights of the European Union. Signed and proclaimed by the Presidents of the European Parliament, the Council and the Commission at the European Council meeting in Nice on 7 December 2000. Retrived October 5, 2003, from http://www.europarl.eu.int/charter/default_en.htm

Child Protection Act, Republic of Estonia. Passed 8 June 1992, entered into force 1 January 1993, last amended 28 January 1998. Retrieved October 5, 2003, from http://www.legaltext.ee/et/andmebaas/ava.asp?m=022

Convention on Human Rights and Biomedicine. Done at Oviedo, Spain, April 4, 1997. Retrieved October 5, 2003, from http://www.oup.co.uk/pdf/bt/cassese/cases/part3/ch16/1121.pdf

Convention on the Rights of the Child of the United Nations. Adopted on 20 November 1989. Retrieved October 5, 2003, from http://www.unicef.org/crc/crc.htm

Dausset, J. (2001) *Predictive medicine.* In *Ethical eye: the human genome.* Mattei, J.-F., ed. 57–68, Council of Europe Publishing.

Declaration of Helsinki of the World Medical Association. Adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amended by the 29th WMA General Assembly, Tokyo, Japan, October 1975; 35th WMA General Assembly, Venice, Italy, October 1983; 41st WMA General Assembly, Hong Kong, September 1989; 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996; 52nd WMA General Assembly, Edinburgh, Scotland, October 2000. Retrieved October 5, 2003, from http://www.faseb.org/arvo/helsinki.htm

European Commission. (2003) *Genetic data and confidentiality. The Estonian experiment. Expert hearing of prof. Ismini Kriari-Catranis, May 27th 2003, Athens.* In *Opinion on the ethical aspects of genetic testing in the workplace.* Opinion No 18. 28th July 2003. The European Group on ethics in science and new technologies to the European Commission. 73–75, Luxemburg: Office of Official Publications of the European Communities. Available also from http://europa.eu.int/comm/european_group_ethics (retrieved December 17, 2003)

Feinberg, J. (1980) *The child's right to an open future.* In *Whose Child? Children's Rights, Parental Authority, and State Power.* Aiken, W. and LaFollette, H., eds. 124-153, Totowa, NJ: Littlefield, Adams & Co.

Foster, D., ed. (1994) *Manual for research ethics committees. British Paediatric Association. Guidelines for the ethical conduct of medical research involving children.* King's College: London, 13.

Friedman Ross, L. and Moon, M. R. (2000) "Ethical issues in genetic testing of children". *Archives of Pediatrics & Adolescent Medicine* 154, 873-879.

General Part of the Civil Code Act, Republic of Estonia. Passed 27 March 2002, entered into force 1 July 2002. Retrieved October 5, 2003, from http://www.legaltext.ee/et/andmebaas/ava.asp?m=022

Great Britain Advisory Committee on Genetic Testing. (1999) "Genetic research and ethics". *Bulletin of Medical Ethics* 145, 21–24.

Human Genes Research Act, Republic of Estonia. Passed 13 December 2000, entered into force 8 January 2001. Retrieved October 5, 2003, from http://www.geenivaramu.ee/index.php?lang=eng&sub=18&eetika=1

Kaprio, J. (2000) "Genetic epidemiology" *British Medical Journal* 320, 1257–1259.

Law of Obligations Act, Republic of Estonia. Passed 26 September 2001, entered into force 1 July 2002. Retrieved October 5, 2003, from http://www.legaltext.ee/et/andmebaas/ava.asp?m=022

Mason, J. K. and McCall Smith, R. A. (1996) *"Law and medical ethics"*. Tallinn: Juridica, 163–165 (in Estonian).

Medicinal Products Act, Republic of Estonia. Passed 19 December 1995, entered into force 1 April 1996. Retrieved October 5, 2003, from http://www.sam.ee/

National Council on Bioethics in Human Research (1993) *Reflections on Research Involving Children.* National Council: Ottawa.

Nelson, R. M., Botkjin, J. R., Kodish, E. D., Levetown, M., Truman, J. T., Wilfond, B. S., Harrison, M., Porter, I. H. and Steinberg, D. (2001) "Ethical issues with genetic testing in pediatrics". *Pediatrics* 107, 1451–1455.

Nõmper, A.(2002) *Estonian Human Gene Research Act and its implementation.* In *Ethics of human genetics: challenges of the (post) genomic era.* Glasa, J., ed. Proceedings of the International Bioethics Conference, October 23-24, 2002, Bratislava, Slovak Republic. Council of Europe, Strasbourg, Charis – IMEB Fdn. Bratislava, 99–104.

Paulson, H. L. (2002) "Diagnostic testing in neurogenetics. Principles, limitations and ethical considerations". *Neurologic Clinics* 20, 3, 627–646.

Richter, G. and Bacchetta, M. D. (1998) "Interventions in the human genome: some moral and ethical considerations". *Journal of Medicine and Philosophy* 23, 3, 303–317.

The regulation no. 125, passed 17 December 2001 by the Minister of Social Affairs of the Republic of Estonia (in Estonian). Retrieved October 5, 2003, from http://www.geenivaramu.ee/index.php?show=main&lang=est

Twomey, J. G. (2002) "Genetic testing of children: confluence or collision between parents and professionals?" *Advanced Practice in Acute and Critical Care Clinical Issues* 13, 4, 557–566.

Universal Declaration on the Human Genome and Human Rights. Adopted by the General Conference of UNESCO on 11 November 1997. Retrieved October 5, 2003, from http://www.unesco.org/human_rights/hrbc.htm

Wijnberg, B. (2000) *Consent of children and minors.* In *International symposium AMADE – UNESCO on bioethics and the rights of the child. Proceedings, Monaco, 28–30 April.* 105–110.

Working party of the Clinical Genetics Society (UK). (1994) "The genetic testing of children". *Journal of Medical Genetics* 31, 785–797.