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WHITHER PEDIATRIC RESEARCH AND PREDISPOSITION GENETIC TESTING?

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Research in which children undergo genetic testing for predisposition to adult-onset diseases or disorders can lead to a better understanding of these conditions. It can possibly also help encourage early detection and the development of clinical and preventive interventions for those found to be at increased hereditary risk. Increasingly, predisposition testing is becoming part of pediatric genetic research. However, the paucity of normative texts about the conduct of pediatric research using predisposition genetic testing generates complex legal and ethical issues. Drawing on the current texts that govern predisposition genetic testing in research and the norms of pediatric research, we outline points of consensus and divergence as well as recommendations regarding predisposition genetic testing in pediatric research.

For few single gene diseases¹, predisposition genetic tests offer clear predictions because they offer information about whether an asymptomatic individual is a carrier of the mutation which, in 100% of cases, causes a specific disease that will manifest during the individual's life. For most conditions, however, predisposition genetic tests identify an increased susceptibility to a particular disease or, often, to several diseases which form a hereditary syndrome.

In this last case, genetic susceptibility increases the risk of developing the disease(s) often at a younger than usual age of onset². The manifestation of the disease may depend on the interaction of several genes or on environmental factors³. In addition to clinical practice uses, researchers are developing research protocols for genetic testing. Clinical genetic information may be distinguished from research results; research results are likely to be much more uncertain, ambiguous, and may involve tests which have not been clinically validated.

Why an ethical concern about predisposition genetic testing research in pediatrics? Genetics is a rapidly developing area of

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medicine⁴ and, undoubtedly, children will be recruited for research for a variety of reasons: they may come from families with a history of adult-onset diseases who are likely to be considered participants in predisposition genetic testing research; a growing number of diseases are known to have a genetic component⁵; and accumulating evidence demonstrates that risk factors during childhood contribute to several late onset disorders⁶. There are some guidelines about the inclusion of children in research⁷ but very few refer specifically to genetic research.

While individual results are not given in most research environments, the availability of predisposition genetic test results from genetic research can be problematic for a variety of reasons. The relationship between the research finding and the risk of developing a disease may be unclear. As mentioned above, research testing may not have clinical level accuracy. The result may identify either mutations in asymptomatic individuals or a susceptibility to an illness for which there is no known treatment (curative or preventative)⁸. Furthermore, if researchers intend on providing individual results to participants, there is an expectation that, to understand the implications of the individual predisposition test results, subjects should undergo genetic counselling, which in a research environment is not easily accessible. In addition, genetic information is often considered problematic because it reveals both individual and familial information⁹. Also, mere knowledge of hereditary disease predisposition and individual test results can have psychological, social, or financial consequences¹⁰. Even in clinical settings, where the issue is whether to perform predisposition genetic tests on children, several difficult ethical questions are raised, for example, whether, when, and by whom children should be informed about their genetic test results¹¹. Disclosing the results of the tests to parents may contravene the child's right not to know the information (right not to know/right to an open future).

However, predisposition test results may also be beneficial clinically since they can promote targeted screening (if there are

appropriate screening needs), help make informed decisions about carrier status (notably about the question of planning a pregnancy) and help people take control of their health. They can also provide a sense of relief from uncertainty about whether hereditary risks are present, as well as end the need for intensive screening for those without a familial mutation. Tests results can help people prepare psychologically and practically for the future; however, they may also raise uncertainties¹². In short, the legitimacy and acceptability of predisposition testing is dependent on the context and the population involved¹³.

In the clinical setting, the principal justification for the use of predisposition tests in pediatrics is that testing is in the "best interest" of the child. If the test reveals the presence of a deleterious mutation, and there are treatments or effective preventive measures which can be initiated during childhood, this could be clearly beneficial to the child¹⁴. For example, among families considered at-risk due to family history or prior positive test results in affected adult relatives, predisposition genetic testing has been used to identify children carrying a mutation that makes them susceptible to a particular type of colon cancer, familial adenomatous polyposis¹⁵. In this case, the use of predisposition genetic tests is considered legitimate because the cancer may develop before the child reaches the age of majority and also because identification allows for early interventions that reduce morbidity and mortality, such as periodic monitoring and, if the disease develops, earlier treatment. It also stops the monitoring of those not at risk.

More recently, certain national organizations have claimed that it may be legitimate at times to use predisposition testing in the broader context of pediatric research. For example, the American Academy of Pediatrics' guidelines on ethical issues in genetic testing involving children (published in 2001 and reaffirmed in 2004) mention that, while it is necessary to limit the use of genetic tests for late-onset diseases among children, research in this domain should be encouraged¹⁶. Also, the Bioethics Advisory Committee of Singapore has suggested that

genetic tests (without specific reference to genetic predisposition tests) can be carried out on vulnerable populations in a research context when the research is sufficiently important and when it cannot be done without the vulnerable population¹⁷.

With this in mind, we will briefly set out the context in which predisposition testing in pediatric research is useful (I). Then, we will examine the ethical and legal norms concerning the use of these predisposition tests which limit to pediatric research (II). Throughout, we will review whether it is legitimate, according to current normative frameworks¹⁸, to use predisposition tests in pediatric research and, if so, under which conditions. Our analysis focuses on normative texts related to human genetics 1) adopted since 1995, 2) be they international, European, Canadian or American, and 3) specifically address the use of predictive tests in research, or, more generally, genetic research involving children. To conclude, we present our key findings as well as our position on the use of genetic predisposition tests in pediatric research.

I. Context

With respect to children, a fundamental principle in law and ethics is the consideration of the “best interests” of the child¹⁹; this principle should guide decision-making about the child’s care. In pediatric research, this principle is reflected, on one hand, in the duty of special protection for children, while recognizing their specific vulnerability²⁰. For example, their autonomy—i.e. their capacity to make decisions and to protect their own interests—is not completely developed and their ability to comprehend important aspects of research will vary based on their stage of development²¹. On the other hand, it has also been recognized that acting in the best interests of the child means not excluding them from research²². Provided that the potential risks and benefits are balanced, it is generally desirable that research be carried out:

Research directed at childhood and early precursors of adult disease relies on studies occurring during childhood, and as genetic contributors to common complex diseases are

identified, a broader range of conditions will be studied. In addition, study of genetic variation within families is an important methodological approach in genetic research. As a result, children are important participants in genetic research.²³

Today, pediatric research, including genetic research, is considered essential and beneficial for improving the health and well-being of children²⁴. It is useful to examine the normative texts regarding the use of predisposition genetic testing in research and the normative rules governing research participation of children.

II. Normative Frameworks

Is it legitimate to use predisposition tests in pediatric research? If so, in what context? What conditions must be met? Current normative documents do not explicitly focus on the topic of predisposition testing in children²⁵. Thus, in the absence of specific research guidelines, it is important to determine (1) whether the use of predisposition genetic testing in research is generally permissible; and then (2) if there are any special considerations regarding pediatric genetic research that may be applicable to predisposition tests.

1) Predisposition Genetic Testing in Research

Few international or national normative instruments specifically address the issue of using predisposition tests in research, with the exception of: the 1997 *Convention on Human Rights and Biomedicine*²⁶ by the Council of Europe, *Testing for Genetic Predisposition to Adult Onset Disease*²⁷ guidelines by the International Federation of Gynecology and Obstetrics (FIGO), and the *Ethical Issues With Genetic Testing in Pediatrics*²⁸ by the American Academy of Pediatrics’.

Under certain circumstances and conditions, the *Convention on Human Rights and Biomedicine*²⁹ legitimizes the use of predisposition tests (the Convention uses the expression “predictive genetic test”) in medical research:

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 counselling.³⁰

Specifically, according to the explanatory report to the Convention, it is necessary that the research pursue one of the two following goals: develop medical treatment or increase the ability to prevent diseases³¹. However, it is also mentioned that when predisposition tests seek to detect late-onset serious illnesses for which there is no treatment, then the use of these tests must be limited, even in a research context, to exceptional cases. “Exceptional cases” are not defined by either the Convention or the related report and these texts do not contain any additional guidance which might justify the exceptional usage of predisposition tests for research³². The reason for this limitation on the use of predisposition tests is that they risk violating the principles of free participation and of respect for privacy³³. Generally, the Convention specifies that genetic tests can occur only after the individual in question has given his/her consent and after there has been appropriate genetic counselling³⁴. However, the Convention does not specify whether appropriate genetic counselling is applicable in the clinical or research context, or both. Nevertheless, genetic counselling is likely more accessible in a clinical setting³⁵.

The FIGO guidelines provide commentary about the use of certain predisposition tests in research. The guidelines emphasize that no susceptibility test for genetic disease should be done or proposed in the absence of informed consent³⁶. Also, the recommendations acknowledge that obtaining informed consent for predisposition testing is different because of the complex gene-gene and gene-environment interactions that influence the manifestation of the given disease³⁷. However, they do not provide guidance on this issue. Again, pre- and post-test genetic counselling is recommended³⁸. But, as noted in the Convention, this recommendation is primarily applicable for predisposition tests occurring in a clinical setting. FIGO also affirms that the

“[c]onfidentiality of the testing and the results is critical”³⁹. FIGO recommends that researchers indicate to participants that there is the possibility of specifying if they would like to know the results of their genetic predisposition⁴⁰. Yet, in many research environments, the reliability and predictive value of genetic tests are often unknown or unclear and still under development. Nevertheless, FIGO guidelines state that participants “should have the opportunity to designate whether or not genetically related family members should have access to the information if they so desire and if the information could significantly influence their health care”⁴¹.

The guidelines of the American Academy of Pediatrics on the use of genetic testing in children stipulate the need to limit the use of genetic tests for late-onset diseases during childhood, yet uphold the need for research in this area⁴².

Finally, several other normative texts have provided guidelines to frame the use of genetic tests, however, they do not specifically address predisposition genetic tests in research. These more general guidelines will not be discussed in this paper.

2) Pediatric Genetic Research

In pediatric research, the conditions are strict. Research involving children may be undertaken only if 1) the research in question could not take place on an adult population⁴³, 2) the research is being undertaken in the best interests of the child (i.e. likelihood of direct benefit to the child) or, in exceptional cases, for the best interests of the group for which the child is a part⁴⁴, and 3) the legal representative gives free and informed consent for the minor’s participation in the research project in question⁴⁵. Also, in cases where a research project does not directly benefit the child, the research may not expose the child to more than minimal risk⁴⁶. However, it is also controversial whether genetic testing presents minimal risk⁴⁷. Furthermore, the majority of normative texts with articles on the subject of genetic research and minors recognize that, when a

child can understand the nature and consequences of the proposed research⁴⁸, their opinion (assent) to participate in research decisions must be taken into account, and should be based on their age and level of maturity⁴⁹. Some of these same normative texts stress the importance of respecting children's dissent⁵⁰, while others hold that it is necessary to take into account the dissent of minors⁵¹. The notion of hereditary disease risk is very complicated and its interpretation varies greatly among adults⁵². Therefore, the interpretation of hereditary disease risk will likely cause even greater difficulties for children.

Finally, another important issue to consider is confidentiality. Since there are no specific regulations concerning confidentiality or the communication of research results in pediatric research, it seems appropriate to apply the same limits applicable to adult genetic research to pediatric research. It is important to highlight that if there are results to be given at the time or in the future, it is the parent who will receive the results, when the tested subject is a child. This obviates the child's right not to know and raises issues of how and when children should be informed of the availability of this result. Generally, all personal information procured in research is confidential and should be treated in a manner that respects privacy⁵³. Furthermore, research participants do not generally receive individual research results, as the purpose of research is to produce generalized knowledge. However, research participants have the right to be informed of such general results⁵⁴ within a reasonable time⁵⁵. In exceptional cases, where research reveals information which directly impacts on the current or future health of the research participants, informing the participants of the research results should be proposed⁵⁶. However, it can be difficult, in both adult and pediatric genetic research to determine when the results are of clear clinical utility and, even when that is established, to know how to approach participants to ascertain if they are interested in learning their test result, either directly or through further clinical testing. Other complications include the fact that in a context where a result may have medical implications for more than one family

member, the requirement to protect confidentiality may be challenging to balance against the rights of the other family members. Generally, third party access to genetic information is permitted only when the individual consents to this access⁵⁷. Also, it is important to respect the participant's right not to be informed⁵⁸.

Conclusion

The use of predisposition tests in pediatric research is complex because it rarely has a short-term effect on the health of the child. It can be useful and beneficial, in the long-term, for the health of the pediatric population as a whole. However, is this in the best interests of the child?

Based on our analysis of normative texts, it seems that specific protection measures framing the use of predisposition genetic tests in pediatric research are extremely limited. In fact, although there are provisions on the use of predisposition tests in research, they seem aimed principally at research carried out on adults. The guidelines regarding adult research are not sufficient to handle the complexities of children's rights to confidentiality, the right not to know and the right to choose. The need for specific norms that protect the rights and interests of children in research has been long recognized⁵⁹. Moreover, the use of predisposition tests in minors raises specific issues. Consequently, it seems important to develop norms for the use of predisposition tests in pediatric research, particularly regarding questions about the best interests of the child and assent issues.

Regarding assent, the *Convention on the Rights of the Child* states that adults must involve children in decisions that concern them⁶⁰. Though the importance of including minors in the research decision process (assent) is recognized, there is a lack of uniformity as to how this requirement will be satisfied. In this regard, we suggest that the information document and assent process be adapted to the child's language and comprehension level and be separate from the documents and consent process applicable to the parents. Second, considering the amount and the complexity

of the information specific to genetic research, it will be important to take into consideration children's developmental and cognitive levels if research assent is to be expected. Third, there should be periodic review of assent, especially for longitudinal research, as the meaning of particular genetic information is likely to change with time. Overall, we believe that it is important to promote the active participation of young people in research: in other words, as partners in its different stages⁶¹.

It is important that all pediatric research be guided by the best interests of the child, in conformity with the 1989 *Convention on the Rights of the Child*. The duty to act in the best interests of the child requires us to ensure that each child be protected against research risks while also requiring that our actions, or non-actions, do not cause any harm to this population. Pediatric predisposition genetic testing research will probably not provide short-term medical benefits for the health of the child and there are potential psychosocial risks related to the communication of predisposition test results. These issues are noteworthy. We believe that to conform to the standards of the best interests of the child, specific rules are required for the confidentiality of predisposition test results in pediatric research. Moreover, if there are no treatment or effective preventive measures that can benefit the actual or future health of the child, there should be no disclosure of research test results (either to the child or to the parents) for the following reasons: it would not be in the best interests of the child, it would contravene the child's rights to confidentiality and privacy, and it can have psychosocial consequences. However, if and when the predisposition test provides information that can be clinically validated, i.e. when it can be used to improve present and future health, and when the conditions currently governing the use of predisposition genetic tests in minors in the clinical context are met, then the research results should be communicated. In addition, we advocate the use of genetic counselling, prior to the communication of genetic information, and a well developed process of assent.

At the beginning of the 1990s, the clinical use of predisposition genetic tests in the pediatric population received relatively little attention in the literature⁶² and in ethical and professional norms⁶³. Today that situation has changed⁶⁴. While the imperative for pediatric genetic research is there, none of the normative texts examined explicitly address the question of the use of predisposition tests in pediatric research⁶⁵. We believe that there is a need for the development of guidelines specifically geared to the rights and interests of children as participants in genetic research.

¹ For example, in Huntington Chorea. (M. HUG et M.R. HAYDEN, "Huntington Disease", in *Gene Reviews*, University of Washington, Seattle, 1998, [online] www.genetests.org; E. LÉVESQUE, B.M. KNOPPERS, D. AVARD, "La génétique et le cadre juridique applicable au secteur de la santé: examens génétiques, recherche en génétique et soins innovateurs", (2004) 64 *Revue du Barreau*, 75; A. DURR, M. GARGIULI, J. FEINGOLD, "Les tests présymptomatiques en neurogénétique", (2005) 21(11) *Médecine Sciences*, 934, 936

² Such as in the case of certain cancers (breast cancer, ovarian cancer, or colon cancer) (A.F. PATENAUE, *Genetic Testing for Cancer: Psychological Approaches for Helping Patients and Families*, American Psychological Association, Washington, 2005, p. 42, 130, 230; M.L. DI PIETRO, A. GIULI, A.G. SPAGNOLO, "Ethical implications of predictive DNA testing for hereditary breast cancer", (2004) *Annals of Oncology* 15 (Supplement 1): i65)

³ D.W. SCHWERTZ et K.M. McCORMICK, "The Molecular Basis of Genetics and Inheritance", (1999) 13(4) *J. Cardiovasc. Nurs.*, 1

⁴ A.E. GUTTMACHER, F.S. COLLINS, "Realizing the Promise of Genomics in Biomedical Research", (2005) 294(11) *JAMA*, 1399-1402

⁵ A.E. GUTTMACHER, F.S. COLLINS, R.H. CARMONA, "The Family History – More Important Than Ever", (2004) 351(22) *N Engl J Med*, 2333-2336

⁶ G.S. BERENSON, S.R. SRINIVASAN, W. BAO et al., "Association Between Multiple Cardiovascular Risk Factors and Atherosclerosis in Children and Young Adults: The Bogalusa Heart Study", (1998) 338 *New England Journal of Medicine*, 1650-1656; C.S. BERKEY, A.L. FRAZIER, J.D. GARDNER, G.A. COLDITZ, "Adolescent and Breast Cancer Risk", (1999) 85 *Cancer*, 2400-2409; J. ZIEGLER, "Exposure and Habits Early in Life May Influence Breast Cancer Risk", (1998) 90 *Journal of National Cancer Institute*, 187-188

⁷ See notably: Council for International Organizations of Medical Sciences (CIOMS) [in Collaboration with the World Health Organization (WHO)], *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, Geneva, 2002, guidelines 13-15

⁸ F. MARGARET, A. OTLOWSKI, R. WILLIAMSON, "Ethical and Legal Issues and the "New Genetics", (2003) 178(11) *MJA*, 582

⁹ S. TAUB, K. MORIN, M. A. SPILLMAN, R. M. SADE, F. A. RIDDICK, [Council on Ethical and Judicial Affairs of the American Medical Association], "Managing Familial Risk in Genetic Testing", (2004) 8:3 *Gene Test*, 356-359

¹⁰ R.E. DUNCAN, J. SAVULESCU, L. GILLAM, R. WILLIAMSON, M.B. DELATYCKI, "An International Survey of Predictive Genetic Testing in Children for Adult Onset Conditions", (2005) 7: 6, *Genetics in Medicine*, 390; A. CLARKE, F. FLINTER, "The Genetic Testing of Children: a Clinical Perspective", in T. Marteau, M. Richards (eds), *The Troubled Helix: Social and Psychological Implications of the New Human Genetics*, Cambridge University Press, 1996, p. 164-176; J.SAVULESCU, "Predictive Genetic Testing in Children", (2001) 175 *MJA*, 379-381

¹¹ E. NELSON, K. HAYMOND, M. SIDAROUS, "Selected Legal and Ethical Issues Relevant to Pediatric Genetics", (1998) 6 *Health Law Journal*, 83, 106-107

¹² A. F. PATENAUE, *Genetic Testing for Cancer: Psychological Approaches for Helping Patients and Families*, op. cit. note 2, p. 12-13

¹³ In fact, it is generally recognized that the issues raised by the use of predictive tests in minors are different than those raised by the use of predictive tests in adults. For more on this topic, see particularly R.E. DUNCAN, M.B. DELATYCKI, "Predictive Genetic Testing in Young People for Adult-Onset Conditions: Where is the Empirical Evidence?", (2006) 69 *Clin Genet*, 9

¹⁴ See notably: World Medical Association, "Statement on Genetics and Medicine", Santiago, 2005, art. 10; Canadian Pediatric Society, "Guidelines for genetic testing of healthy children", (2003) 8(1) *Paediatr Child Health*, 51; American Academy of Pediatrics (AAP), "Ethical Issues With Genetic Testing in Pediatrics", (2001) 107(6) *Pediatrics*, 1451 [reaffirmed by the American Academy of Pediatrics (AAP), "AAP Publications Retired and Reaffirmed", (2005) 115(5) *Pediatrics*, 1438; American Society of Human Genetics (ASHG)/American College of Medical Genetics (ACMG), "Points to Consider: Ethical, Legal and Psychological Implications of Genetic Testing in Children and Adolescents", (1995) 57 *American Journal of Human Genetics*, A1, A3; American Medical Association (AMA), "E-2.138 Genetic Testing of Children", 1995, [online] <http://www.ama-assn.org/ama/pub/category/print/8439.html>; American Society of Clinical Oncology, "Policy Statement Update: Genetic Testing of Cancer Susceptibility", (2003) 21(12) *Journal of Clinical Oncology*, 1, 4; B.M. KNOPPERS, D. AVARD, G. CARDINAL, K.C. GLASS, "Children and Incompetent Adults in Genetic Research: Consent and Safeguard", (2002) 3(3) *Science and Society*, 221-224; R. E. DUNCAN, J. SAVULESCU, L. GILLAM, R. WILLIAMSON, M.G. DELATYCKI, "An International Survey of Predictive Genetic Testing in Children for Adult Onset Conditions", loc. cit. note 10, 390; A.F. PATENAUE, *Genetic Testing for Cancer: Psychological Approaches for Helping Patients and Families*, op. cit. note 2, p. 241-243; G. GELLER, "The Ethics of Predictive Genetic

Testing in Prevention Trials Involving Adolescents", in E. Kodish (ed), *Ethics and Research with Children – A Case-Based Approach*, 2005, Oxford University Press, p.195; J. SAVULESCU, "Predictive Genetic Testing in Children", loc. cit. note 10, 379-381

¹⁵ For more information, see A. F. PATENAUE, *Genetic Testing for Cancer: Psychological Approaches for Helping Patients and Families*, op. cit. note 2, p. 243-244

¹⁶ American Academy of Pediatrics (AAP), "Ethical Issues With Genetic Testing in Pediatrics", loc. cit. note 14

¹⁷ Bioethics Advisory Committee, *Genetic Testing and Genetic Research*, Appendix D: *Ethical, Legal and Social Issues in Genetic Testing and Genetics Research: a Consultation Paper*, Singapore, April 5, 2005, p. 14

¹⁸ We refer, by the concept of normative framework, to a broad notion, synonymous with the concept of "champ normatif" (normative field) defined as :

"not only the elaboration of a juridical texts strictly defined, but also the totality of non-legal or sub-legal including ethical, political and economic rules, informal or implicit rules based on practice, discourse, and custom that also participate in regulating biotechnologies" [unofficial translation]". (P. PEDROT, "Éthique médicale et norme nationale", dans D. FOLSCHEID, B. FEUILLET-LEMINTIER et J.-F. MATTEI (dir.), *Philosophie, éthique et droit de la médecine*, Paris, Presses Universitaires de France, 1997, p. 262)

¹⁹ United Nations (High Commissioner for Human Rights), *Convention on the Rights of the Child*, 1989, art. 3(1)

²⁰ L.H. GLANTZ, "Research with Children", (1998) 24 *American Journal of Law and Medicine*, 218; M. EDER, "Testing Drugs in Developing Countries: Pediatric Research Ethics in an International Context", in E. Kodish (ed), *Ethics and Research with Children – A Case-Based Approach*, op. cit. note 14, p. 243

²¹ D. AVARD, B. M. KNOPPERS, "Screening and Children: Policy Issues for the New Millennium", (2001) 2(3) *ISUMA*, 46-55

²² B. M. KNOPPERS, D. AVARD, G. CARDINAL et K. C. GLASS, "Children and Incompetent Adults in Genetic Research: Consent and Safeguards", (2002) 3(3) *Science and Society*, 221; T. ST-LAURENT, "La recherche clinique et les enfants en soins palliatifs : normes et enjeux éthiques", Doctoral thesis, Faculty of medicine – biomedical sciences, 2006, p. 19-20, 22, 38; A. LYNCH, "Research Involving Children : Why not? ", (1999) 32 *Annales CRMCC*, 128-132; H. DOUCET, "L'expérimentation sur les enfants", dans G. DURAND, C. PERROTIN (Éds), "Contribution à la réflexion bioéthique: Dialogue France-Québec", Éditions Fides, Québec, 1991, p. 119-131

²³ W. BURKE, D. S. DIEKEMA, "Ethical Issues Arising from the Participation of Children in Genetic Research", (2006) *Journal of Pediatrics*, S34

²⁴ Royal College of Pediatrics and Child Health: Ethics Advisory Committee, "Guidelines for the Ethical Conduct of Medical Research Involving Children", (2000) *Arch Dis Child* 82, 177-182

²⁵ It is nevertheless necessary to specify that our analysis is limited to normative texts that fit the criteria described in the introduction

²⁶ Council of Europe, *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine* (hereafter, *Convention on Human Rights and Biomedicine*), Oviedo, April 4, 1997, [online] <http://conventions.coe.int/Treaty/EN/Treaties/Html/164.htm>

²⁷ The International Federation of Gynecology and Obstetrics (FIGO) is an international professional organization that frames modern practices in research and medicine. FIGO published a collection of recommendations regarding the ethical problems in human reproduction and aims to support, among other things, an awakening of responsibility for new medical and research practices. (International Federation of Gynecology and Obstetrics (FIGO), *Recommendations on Ethical Issues in Obstetrics and Gynecology by the FIGO: Committee for the Study of Ethical Aspects of Human Reproduction*, London, November 2003, [online] http://www.figo.org/content/PDF/ethics-guidelines-text_2003.pdf;

N. LENOIR and B. MATHIEU, *Les normes internationales de la bioéthique*, Que sais-je?, Paris, Presses Universitaires de France, 1998, p. 28-29)

²⁸ American Academy of Pediatrics (AAP), "Ethical Issues With Genetic Testing in Pediatrics", loc. cit. note 14

²⁹ The Convention is an international normative document which is applicable in the countries that have ratified it. Although this instrument has been adopted by the Council of Europe's Parliamentary Assembly (which makes it, at first view, seem to have regional scope), it is necessary to note that this instrument is open to the signatures and ratification of non-member countries of the Council of Europe (Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 33 al. 1 and art 34 al. 1); this could give it an international reach (for the countries which committed to it through ratification because its effectiveness depends on states' decisions to ratify or not to ratify it)

³⁰ Indeed, predictive tests cannot be carried out except for medical reasons or for medical research (Council of Europe, *Convention on Human Rights and Biomedicine*, art. 12), unless a national law does not permit them for

the necessary reasons, in a democratic society, of public safety, to prevent penal infractions, or to protect public health or the rights and freedoms of others. (COUNCIL OF EUROPE, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 26.1)

³¹ Council of Europe, *Explanatory Report to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, Strasbourg, Directorate of Legal Affairs, January 1 1997, art. 12, paragraph 82

³² Nevertheless, it is interesting to note that the “Working Party on Human Genetics,” a working group affiliated with the Council of Europe’s Steering Committee on Bioethics, published a working document in which it specified that predictive genetic tests could be used on people, among others, for scientific research ends if the research is related to health. (Working Party on Human Genetics, (CDBI-Council of Europe), *Working Document on the Applications of Genetics for Health Purposes*, Strasbourg, February 7, 2003, art. 15 [online] http://www.coe.int/T/E/Legal_affairs/Legal_co-operation/Bioethics/Activities/Human_genetics/INF%282003%293E_Wkg_doc_genetics.pdf)

³³ Council of Europe, *Explanatory Report to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, op. cit. note 31, art. 12, paragraph 81

³⁴ Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, article 12; Council of Europe, *Explanatory Report to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, op. cit. note 31, art. 12, paragraph 88

³⁵ G. RENEGAR, C.J. WEBSTER, S. STUERZEBECHER, et al., “Returning Genetic Research Results to Individuals: Points-to-Consider”, 2006 20(1) *Bioethics*, 24-36

³⁶ International Federation of Gynecology and Obstetrics (FIGO), “Testing for Genetic Predisposition to Adult-Onset Disease,” Recommendation 1, in the International Federation of Gynecology and Obstetrics (FIGO) *Recommendations on the Ethical Issues in Obstetrics and Gynecology by the FIO Committee for the Ethical Aspects of Human Reproduction and Women’s Health*, London, November 2003, [online] http://www.figo.org/content/PDF/ethics-guidelines-text_2003.pdf

³⁷ *Id.*

³⁸ *Id.*, Recommendation 3

³⁹ *Id.*, Recommendation 4

⁴⁰ *Id.*, Recommendation 5

⁴¹ *Id.*

⁴² American Academy of Pediatrics (AAP), “Ethical Issues With Genetic Testing in Pediatrics”, *loc. cit.* note 14

⁴³ United Nations Educational, Scientific and Cultural Organization (UNESCO), *Universal Declaration on Bioethics and Human Rights*, Paris, October 19, 2005, art. 7(b); United Nations Educational, Scientific and Cultural Organization (UNESCO), *Declaration on the Human Genome and Human Rights*, Paris, November 11, 1997, art. 5(e); Council For International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, op. cit. note 7, guidelines 13 and 14; Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 17(1)(iii); Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, Strasbourg 2005, art. 15(1)(ii); Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, Ottawa, Minister of Supply and Services Canada, 1998 (updated in 2000, 2002 and 2005), article 2.5(1)

⁴⁴ United Nations Educational, Scientific and Cultural Organization (UNESCO), *Universal Declaration on Bioethics and Human Rights*, op. cit. note 43, art. 7(a), 7(b); United Nations Educational, Scientific and Cultural Organization (UNESCO), *Declaration on the Human Genome and Human Rights*, op. cit. note 43, art. 5(b), 5(e); Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, op. cit. note 7, guidelines 13 and 14; Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 6(1), 17(1)(ii), 17(2)(i); Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, op. cit. note 43, art. 15(1)(i), 15(2)(i); European Commission, *25 Recommendations on the ethical, legal and social implications of genetic testing*, Brussels, 2004, recommendation 25(a); Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, op. cit. note 43, article 2.5(a), 2.5(c) and 5.3.

⁴⁵ United Nations Educational, Scientific and Cultural Organization (UNESCO), *Universal Declaration on Bioethics and Human Rights*, op. cit. note 43, art. 7; United Nations Educational, Scientific and Cultural

Organization (UNESCO), *Declaration on the Human Genome and Human Rights*, op. cit. note 43, art. 5(b); Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, op. cit. note 7, guidelines 13 and 14; Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 17(1)(iv); Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, op. cit. note 43, art. 15(1)(iv); Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, op. cit. note 43, article 2.5(b) and 2.6

⁴⁶ United Nations Educational, Scientific and Cultural Organization (UNESCO), *Universal Declaration on Bioethics and Human Rights*, op. cit. note 43, art. 7(b); United Nations Educational, Scientific and Cultural Organization (UNESCO), *Declaration on the Human Genome and Human Rights*, op. cit. note 43, art. 5(b); Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, op. cit. note 7, guideline 13; Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 17(2)(ii); COUNCIL OF EUROPE, *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, op. cit. note 43, art. 15(2)(ii); Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, op. cit. note 43, article 2.5(c)

⁴⁷ J. F. MERZ, “Is Genetics Research “Minimal Risk”?”, (1996) 18(6) *IRB*, 7-8; S. COX, “Assessing Risk Assessment: Genetic Testing and Screening for Complex Disease”, (2006) 70(5) *Clin. Genet.*, 438-444

⁴⁸ Acquiring autonomy is a process of development; it is acquired alongside children’s gradual development of cognitive capacities and moral reasoning. (D. AVARD, B. M. KNOPPERS, “Screening and Children: Policy Issues for the New Millennium”, *loc. cit.* note 21, 48)

⁴⁹ United Nations Educational, Scientific and Cultural Organization (UNESCO), *Universal Declaration on Bioethics and Human Rights*, op. cit. note 43, art. 7(a); Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, op. cit. note 7, guideline 14; Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 6(2); Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, op. cit. note 43, art. 15(1)(iii), 15(1)(iv), 15(1)(v); European Commission, *25 Recommendations on the ethical, legal and social implications of genetic testing*, op. cit. note 44, recommendation 25(b); Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, op. cit. note 43, article 2.7

⁵⁰ United Nations Educational, Scientific and Cultural Organization (UNESCO), *Universal Declaration on Bioethics and Human Rights*, op. cit. note 43, art. 7(b); Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, op. cit. note 7, guideline 14; Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 17(1)(v); Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, op. cit. note 43, article 2.7

⁵¹ Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, op. cit. note 43, art. 15(1)(iv); European Commission, *25 Recommendations on the ethical, legal and social implications of genetic testing*, op. cit. note 44, recommendation 25(b)

⁵² A.F. PATENAUDE, *Genetic Testing for Cancer: Psychological Approaches for Helping Patients and Families*, op. cit. note 2, p. 118-121

⁵³ United Nations Educational, Scientific and Cultural Organization (UNESCO), *Universal Declaration on Bioethics and Human Rights*, op. cit. note 43, art. 2(d), 9; United Nations Educational, Scientific and Cultural Organization (UNESCO), *Declaration on the Human Genome and Human Rights*, op. cit. note 43, art. 7; Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, op. cit. note 7, guideline 18; Council of Europe, *Convention on Human Rights and Biomedicine*, op. cit. note 26, art. 10; Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, op. cit. note 43, art. 25(1), 26(1), 26(2); Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, op. cit. note 43, chapter 3; Network of Applied Genetic Medicine (RMGA), *Statement of Principles: Human Genome Research – version 2000*, Montreal, 2000, principle III

⁵⁴ Most of the normative texts framing genetic research assert the right to access general research results. (Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research*, *op. cit.* note 43, art. 28(2); Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, Ottawa, Minister of Supply and Services Canada, *op. cit.* note 43, article 8.1; Network of Applied Genetic Medicine (RMGA), *Statement of Principles: Human Genome Research – version 2000*, *op. cit.* note 53, principle II.(4)

⁵⁵ Council of Europe, *Protocol to the Convention on Human Rights and Biomedicine, on Biomedical Research*, *op. cit.* note 43, art. 28, Network of Applied Genetic Medicine (RMGA), *Statement of Principles: Human Genome Research – version 2000*, *op. cit.* note 53, principle II

⁵⁶ Council of Europe, *Protocol to the Convention on Human Rights and Biomedicine, on Biomedical Research*, *op. cit.* note 43, art. 27; Network Of Applied Genetic Medicine (RMGA), *Statement of Principles: Human Genome Research – version 2000*, *op. cit.* note 53, principle II(4) and III(2)

⁵⁷ NETWORK OF APPLIED GENETIC MEDICINE (RMGA), *Statement of Principles: Human Genome Research – version 2000*, *op. cit.* note 53, principle III al. 2. For example, it is stimulated that, in exceptional circumstances, a researcher can disclose genetic information to the members of a participant's biological family, without the participant's consent. Three conditions must be met for this to take place: 1) when non-disclosure is likely to involve serious and foreseeable damage to the biological family; 2) when members of the biological family are identifiable; and 3) when the risk of prejudice can be avoided through prevention or control by an approved scientific treatment. Also, it specifies that an evaluation of disclosure or non-disclosure of the genetic information to the participant's biological family must take into account that the prejudice caused by the disclosure must not be greater than the prejudice caused by non-disclosure. (RMGA, principle III)

⁵⁸ United Nations Educational, Scientific, and Cultural Organization (UNESCO), *Declaration on the Human Genome and Human Rights*, *op. cit.* note 43, art. 5(c); Council of Europe, *Convention on Human Rights and Biomedicine*, *op. cit.* note 26, art 10(2); Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine, on Biomedical Research*, *op. cit.* note 43, art. 27; Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*, *op. cit.* note 43, article 8.1; Network of Applied Genetic Medicine (RMGA), *Statement of Principles: Human Genome Research – version 2000*, *op. cit.* note 53, principle II

⁵⁹ For example, World Medical Association, *Declaration of Helsinki*, Edinburgh, October 2000, principle A.8; Council of International Organizations Of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, *op. cit.* note 7, guideline 13

⁶⁰ "States Parties shall assure to the child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child, the views of the child being given due weight in accordance with the age and maturity of the child". United Nations (Office of the High Commissioner for Human Rights), *Convention on the Rights of the Child*, *op. cit.* note 19, art. 12 al. 1

⁶¹ INVOLVE, *A Guide to Actively Involving Young People in Research: For Researchers, Research Commissioners, and Managers*, United Kingdom, September 2004

⁶² M. BLOCH, M.R. HAYDEN, "Opinion: Predictive Testing for Huntington Disease in Childhood and Implications", (1990) 46 *American Journal of Human Genetic*, 14; A. CLARKE, "The Genetic Testing of Children", Working Party of the Clinical Genetics Society (UK), (1994) 31 *J Med Genet*, 785-797; D.E. HOFFMANN, E.A. WULFSBERG, "Testing Children for Genetic Predisposition: Is it in their Best Interest ?", (1995) 23 *Journal of Law, Medicine and Ethics*, 331-344

⁶³ The majority of normative texts governing predictive tests in children in the clinical context appeared towards the middle of the 1990s and even in the early years of 2000 (R.E. DUNCAN, M.B. DELATYCKI, "Opinion-Predictive Genetic Testing in Young People for Adult-Onset Conditions: Where is the Empirical Evidence?", *loc. cit.* note 13, 9). For example: American Society of Human Genetics (ASHG)/American College of Medical Genetics (ACMG), "Points to Consider: Ethical, Legal and Psychological Implications of Genetic Testing in Children and Adolescents", *loc. cit.* note 14, 1233-1241; American Academy of Pediatrics (AAP), "Ethical Issues With Genetic Testing in Pediatrics", *loc. cit.* note 14; Canadian Pediatric Society, "Guidelines for Genetic Testing of Health Children", *loc. cit.* note 14, 51

⁶⁴ Notably, see American Medical Association (AMA), "E-2.138 Genetic Testing of Children", *loc. cit.* note 14; World Health Organization (WHO), *World Health Organization Proposed International Guidelines on Ethical Issues in Medical Genetics and the Provision of Genetic Services*, Geneva, 1998; Human Genetic Society of Australasia (HGSA), *DNA*

Presymptomatic and Predictive Testing for Genetic Disorders, 2002; Canadian Pediatric Society, "Guidelines for Genetic Testing of Health Children", *loc. cit.* note 14, 51; European Society of Human Genetics, "Provision of Genetic Services in Europe: Current Practices and Issues – Recommendations of the European Society of Human Genetics", (2003) 11 *supp.2 European Journal of Human Genetics*, S2-S4; American Society of Clinical Oncology, "American Society of Clinical Oncology Policy Statement Update: Genetic Testing for Cancer Susceptibility", *loc. cit.* note 14, 2397-2406; Human Genetic Society of Australasia, *Predictive Testing in Children and Adolescents*, 2005

⁶⁵ American Academy of Pediatrics (AAP), "Ethical Issues With Genetic Testing in Pediatrics", *loc. cit.* note 14; Bioethics Advisory Committee, *Genetic Testing and Genetic Research*, Annex D: *Ethical, Legal and Social Issues in Genetic Testing and Genetics Research: a Consultation Paper*, *op. cit.* note 17, p. 14