

International Bioethics Committee (IBC)
Social and Human Sciences Sector, UNESCO
1, rue Miollis
75732 Paris Cedex 15
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31 July 2014

Dear Sir / Madam

Re: Concept note on updating the IBC's reflection of the human genome and human rights

Introduction

- 1 I am writing on behalf of the Nuffield Council on Bioethics, an independent UK body that examines and reports on ethical issues in biology and medicine, in response to the invitation to feedback on the potential areas of reflection outlined in the concept note.
- 2 The comments made in this document are based on findings of two comprehensive inquiries carried out by the Council in recent years:
 - Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age – *inquiry carried out from 2009- 2010 and the report is published at:* <http://www.nuffieldbioethics.org/personalised-healthcare-0>
 - Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review *was carried out from 2011 – 2012 and is published at:* <http://www.nuffieldbioethics.org/mitochondrial-dna-disorders> (*this work is cited at Paragraph 14 of the concept note*).
- 3 We believe that conclusions and recommendations made in these reports are relevant to the discussions of the IBC in two of the areas of reflection set out on the concept note: on direct to consumer tests and on nuclear transfer to avoid mitochondrial diseases.

Yours sincerely



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Direct to consumer tests (DTC tests)

- 4 The comments in this section are based on the Council's report *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age* (<http://www.nuffieldbioethics.org/personalised>). This report was produced by an interdisciplinary expert Working Party. In coming to its conclusions the Working Party consulted with a wide range of people including those involved in the development, regulation and commercialisation of direct to consumer tests, expert scientists and medical practitioners. Paragraph numbers in brackets refer to paragraph numbers in the Council's report.
- 5 The cost of genetic analysis over the past decade has fallen to the point where genetic profiling services are readily affordable to people with average incomes in developed countries. We therefore need to consider how these services are promoted, how accurate the tests are, how useful the results are, the associated benefits and harms, and the ethical dilemmas they raise (paragraph 9.1).
- 6 Potential benefits and harms of personal genetic profiling for disease susceptibility include:

Potential advantages:
 - More information;
 - allows early intervention;
 - allows more personal control;
 - possibility of saving public healthcare resources if testing and treatment conducted privately; and
 - can alert relatives to important genetic conditions.
Potential disadvantages:
 - Costs to individuals of tests that yield little determinate information;
 - social harms when private testing can undermine equal access to healthcare;
 - costs of consequences of having information: a) for individual when inaccurate or hard to interpret, b) for individual when nothing can be done, c) for individual if inaccurate risk
 - assessments lead to false reassurance or misplaced anxiety, d) for individual if results lead to stigma or information abuse (e.g. blackmail) or other effects that may be regretted, given that information once known cannot be 'un-known' (e.g. for insurance declarations), e) for taxpayers when unnecessary follow-up testing and treatment is carried out;
 - costs and harms to third parties – when children or third parties are tested without consent, or when embryos are tested for conditions whose risks may be hard to determine; and
 - can change perception of wellness and illness through medicalisation of normal variation, including for children (paragraph 9.6).
- 7 Much research is ongoing in this area but there is little evidence yet about the extent of benefits or harms that are actually incurred or accrued through these tests. Moreover, scientists commonly assert that it is difficult to use the results that have emerged so far to make accurate predictions from a genome sequence alone about a person's risk of developing a disease that is caused

by multiple genetic and other lifestyle factors. In addition, results from such studies are specific to the population upon which they were carried out (for example people designated 'Caucasian'), and therefore may not be relevant for people from outside such populations who have these tests. Problems of replicability are also commonly encountered with these studies (paragraph 9.8).

- 8 Further questions arise about whether the results of direct-to-consumer profiling for susceptibility to multifactorial diseases enable the person tested to do anything specifically useful to counteract the possible harm about which they have been warned. For example, are there any preventive measures or therapies they can take to remove, reduce or defer the risk of disease? The risk predictions given generally do not greatly differ from the average risk levels. They also relate to overall lifetime risk and give no indication of when any potential disease will develop, or how severe it might be. It is therefore not generally possible to take specific actions in response to direct-to-consumer predictive genetic profiling beyond those that would result in healthier lifestyles for anybody, such as to maintain a healthy lifestyle (paragraph 9.14).
- 9 Three key points noted in the concept document, and that the Council agrees are central to the debate are: that providers generally do not offer genetic counselling; these tests can produce results that are unreliable or difficult to interpret; and there is no overarching system of regulation for these tests (not least because direct-to-consumer DNA profiling companies can offer their services to customers based anywhere in the world and as such may be operating under a jurisdiction different from that applying where their customers live).
- 10 The existing system of interventions does not promote the provision of good information to consumers about the type of genetic profiling for susceptibility for common diseases offered directly to consumers. There is also a lack of evidence of potential harms and benefits that may result from taking these tests. In the absence of such evidence, we find it problematic that parents are able to order the type of profiling we focus upon for their children.
- 11 In response to these concerns the Council made a number of recommendations:
 - Responsible authorities and regulators should request evidence for the claims being made by companies about the clinical validity of their tests (paragraph 9.45).
 - Independent research on the health and psychological impact and effects of multifactorial genetic susceptibility testing on individuals, including children, should be carried out by public healthcare systems. Such research should include investigation into how many people are purchasing this type of analysis, and the results of this research should be made easily accessible (paragraph 9.47).
 - Government websites should provide information about the risks and benefits of personal genetic profiling, including the relevance for insurance (paragraph 9.49).

- Companies should voluntarily provide clear information on the limitations of genetic profiling and what will happen to people's data (paragraph 9.51).
- Companies should require their customers at the point of sale to click on a statement confirming that they have the consent of the person whose DNA they intend to have analysed, or have parental responsibility in the case of children. Where people live in countries such as the UK where procuring someone else's biological sample for DNA analysis without their knowledge is a legal offence, this statement should also require confirmation that the customer has understood this fact. This agreement should be stated in clear language and separated from other terms and conditions (paragraph 9.53).
- Companies should not knowingly analyse the DNA of children unless certain criteria are met (paragraph 9.54).
- Healthcare professionals should be trained on giving advice to patients about commercial genetic profiling services (paragraph 9.58).
- Genetic profiling companies should provide details about what would happen to personal genetic data and interpretations should the company go into administration or change hands. This information should be made available to consumers before they buy (paragraph 9.60).

Nuclear transfer to avoid mitochondrial diseases

- 12 Pronuclear transfer and maternal spindle transfer are not currently permitted for treatment use under UK legislation. However, draft regulations that would allow the use of these techniques in treatment, subject to a favourable Parliamentary vote, have been developed by the Department of Health. The regulations were sent out for consultation during spring 2014, eliciting more than 1,850 responses. Following the consultation, in July 2014 the Department announced that plans to introduce new legislation will progress and an update will be provided by early autumn.
- 13 In order to ensure that the ethical considerations were fully aired before the UK Parliament debates this issue, and to help inform that process, the Council conducted a six-month inquiry into the ethical issues raised by new techniques that aim to prevent the transmission of maternally-inherited mitochondrial DNA disorders. To assist with this enquiry, the Council appointed a Working Group with varied expertise, including in science, medicine, philosophy and ethics. The Working Group took evidence from and met people representing a wide range of opinion. Its report was published in June 2012 (<http://www.nuffieldbioethics.org/mitochondrial-dna-disorders>).
- 14 The Council concluded that due to the health and social benefits to individuals and families of living free from mitochondrial disorders, and where potential parents express a preference to have genetically-related children, on balance we believe that if these novel techniques are adequately proven to be acceptably safe and effective as treatments, it would be ethical for families to use them, if they wish to do so and have been offered an appropriate level of information and support.

- 15 Subject to the appropriate oversight, we believe that as a research objective it is ethical to gather further information about pronuclear transfer and maternal spindle transfer in order that they can be considered for treatment use.
- 16 We believe that in the first instance, novel techniques such as pronuclear transfer and maternal spindle transfer (or any comparable future treatment) should only be offered as part of a research trial in centres specialising in mitochondrial disorders. Consent to follow up would need to be included as a mandatory part of parental consent to participation in the trial.
- 17 With regard to regulation and follow up, we think it vital that families using such techniques should commit to allowing very long term follow-up of their children and families in order to further knowledge about the outcomes of these techniques. To support this aim we would recommend the creation of a centrally funded register of any such procedures performed in the UK (or indeed, elsewhere), accessible to researchers over several decades.
- 18 With regard to the parentage of the child: although the perception of the personal and social relationships created by egg or embryo reconstruction would be essentially a matter for the individuals concerned, the Council's view is that mitochondrial donation does not indicate, either biologically or legally, any notion of the child having either a 'third parent', or 'second mother'. We find the 'three parent baby' framing of this issue unhelpful to balanced public debate.
- 19 The donor of mitochondria should not have the same status in regulation as a reproductive egg or embryo donor in all aspects. As part of this, we do not believe mitochondrial donors should be mandatorily required to be identifiable to the adults born from their donation.
- 20 The Council concluded that donation treatments for mitochondrial disorders would constitute a form of germline gene therapy. However, there is a clear line between these particular techniques and germline therapies that would act on the nuclear genome. These would involve further ethical considerations and would need to be considered entirely separately. We recommend that the wider policy debate could benefit from a fuller discussion of the ethics of the different kinds of prospective and theoretical germline therapies than those for avoiding mitochondrial disease. This would include potential therapies that would act on the cell nucleus with heritable effects, and therapies which might involve nuclear transfer in its various forms.