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A Common Framework of Principles for direct-to-consumer genetic testing services

Response from the PHG Foundation

Introduction

The Foundation for Genomics and Population Health (PHG Foundation) is the successor body to the Public Health Genetics Unit. Its overarching purpose is to foster and enable the application of biomedical science, particularly genome-based technologies, for the benefit of human health. Among its specific objectives is the promotion of a social and regulatory environment that is receptive to innovation, without imposing an undue or inequitable public burden. The Foundation has a particular interest in the way that new technologies are translated within health services, in genetic research and its impact upon clinical and public health services.

We have structured this consultation response into two sections:

A. General comments and recommendations relating to our position on DTC genetic tests and their regulation;

B. Answers to the specific consultation questions.

A. General Comments

The PHG Foundation recognises that recent technological advances in genomic analysis, information technology and internet-based communication have catalysed the development of a small market in direct-to-consumer (DTC) genetic tests. The blend of increasingly complex and predictive genomic information coupled with international data sharing and transfer has resulted in a distinctive challenge to regulators of genetic tests across all jurisdictions. We therefore welcome this initiative from the Human Genetics Commission, which seeks to establish a set of general principles of '*best practice*' that will '*promote high standards and consistency*' across the gamut of genetic and genomic tests available DTC worldwide.

In general, we are supportive of a broadly liberal approach favouring regulation primarily through non-legislative mechanisms, provided that proposed uses can be justified as being acceptable in a democratic society and that proportionate safeguards apply[1]. Where the health and safety of consumers is at issue, we advocate the use of statutory safeguards and, unless there are concerns about the safety of such tests, suggest there should be little restriction to making them available in the marketplace. Indeed there is a framework of consumer protection legislation and regulation already in existence which offers some measure of protection to consumers[2]. By contrast, we recognise that where tests are offered by or funded through state providers (such as the NHS or insurers), more rigorous demands should be made of the technologies in terms of effectiveness, cost effectiveness and demonstrable clinical utility, or at the very least, parity with existing technologies. In these circumstances, a higher threshold for regulation may be appropriate.

[1] Burke, W., Zimmern. R., Kroese, M. Defining purpose: a key step in genetic test evaluation *Genetics in Medicine* (2007) Vol 9 (10) 675-681

[2] Such as the Consumer Protection from Unfair Trading Regulations (2008) No.1277 which require that advertising should not make false or misleading claims, particularly as to the risks or benefits of a product marketed DTC.

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Genetic exceptionalism

Our political system and marketplace economy means that there are many products and services which are promoted and sold direct-to-consumer. A complex matrix of consumer protection legislation and regulation already exists which offers some protection to consumers. Since our starting point is that products or services involving genetic analysis or material are not necessarily exceptional, and do not need special treatment simply by virtue of the fact that they are based on analysis of DNA, we do not support legislation that is directed only at such products and services. We prefer the notion that genetic information should be treated the same as any other potentially medically relevant information, and that it should be subjected to *appropriate* levels of protection and privacy. Like other information, the appropriate level of privacy depends upon the context and the type of information: some of it is visible and public (e.g. gender, height, ethnicity, etc.), whilst some is hidden and highly personally sensitive (e.g. *BRCA* status, diagnosis of cancer, treatment details, etc.). The information itself should therefore be regulated in proportion to the level of its sensitivity, relevance to family members and clinical utility, rather than the nature of the test analyte (i.e. DNA) dictating the degree of regulation imposed. We note that there are a number of non-genetic medically relevant tests (e.g. cholesterol level, blood pressure) which are available DTC and may be substantially more predictive than genetic information and have important implications for family members, for which a similar set of guiding Principles does not exist.

That said, we welcome the attempt to define a set of Principles which can be applied systematically and universally across a range of different contexts and applications, and we note that a similar set of Principles might also be useful in other areas of DTC health-related services, such as whole body scans.

We suggest that the HGC considers framing the Principles in a wider context of best practice for all DTC health-related tests and services that are performed on personal in vitro biological samples.

Medical paternalism

We believe that the majority of genetic information does not carry significant medical consequences. Furthermore, we understand that many consumers of genetic tests are not motivated by their advertised medical benefits, but are interested in non-medical applications, such as genealogy testing, for which medical input is unnecessary. Viewed in this light, the Principles could be regarded as being overly paternalistic, requiring a degree of enquiry by the provider of the services that might seem intrusive and inappropriate, and certainly not consistent with other types of tests available on a DTC basis.

We are also concerned about the consequences of formally regulating DTC genomic services, or requiring medical support, where there is insufficient evidence of clinical relevance or usefulness. Rather than simply protecting the consumer from potential harm, it could appear to lend legitimacy to analyses that currently have no medical value and are still areas under active research; recent formal regulation of the homeopathy industry by the MHRA has drawn widespread criticism for exactly this reason[3]. The obvious conclusion is that we should only consider tests that are equivalent to those used clinically as being potentially subject to medical regulation and requiring formal support from qualified clinicians. We do not support 'medicalisation' of the entire genome and do not believe that genome-wide services should be automatically regulated as medical

[3] House of Commons Science and Technology Sub-Committee: "Evidence Check: Homeopathy" (25th November 2009, available at http://www.parliamentlive.tv/Main/Player.aspx?meetingId=5221)

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diagnostic tests, as the majority of the information derived is not clinically relevant. We also note that test providers frequently claim that services are provided on the basis that they are recreational and/or educational rather than a source of medical genetic testing and that tests are not a substitute for medical advice[4]. Nevertheless we recognise that despite these disclaimers, consumers may place considerable reliance on the test results.

We recommend that the Principles be revised to encourage providers ensure that consumers have access to appropriate levels of support to understand their genetic data, and acknowledge that in many cases these sources will be non-medical in origin.

Genome-wide technologies

In the context of standard medical diagnostic tests, the distinction between an *assay* (the scientific measurement of the biomarker of interest) and a *test* (the application of that assay in a particular population, for a particular disease and a specified purpose) is useful for developing and implementing an evaluation framework[5]. However, because of the falling costs of genotyping, a single genotyping assay may in practice produce multiple different test results. For example, a single genome-wide scan using a customised SNP-array may reveal information that is pertinent to susceptibility for multiple complex diseases, carrier status for numerous inherited diseases, pharmacogenetic and nutrigenetic information, ethnicity and ancestry data, and information concerning genetic kinship when compared with another sample.

Therefore the traditional concept of test *purpose* is rather muddied by genome-wide data and it might be difficult to categorise the data arising from a single assay in different ways according to its clinical benefit and apply a range of regulatory strategies; this problem has already occurred in numerous genomic DTC services, and will be greatly exacerbated with the advent of affordable whole genome sequencing, which we expect to be available DTC within the next few years.

We recommend that the Principles explicitly note that multiple types of genetic information may arise from a single genome-wide assay, so separating tests into distinct categories for the purposes of regulation is artificial.

B. Specific Comments on the Consultation Questions

1. **Do you believe that recommending individualised pre- and post-test counselling to accompany genetic tests in the context of inherited or heritable disorders is the right approach?**

   Our view is that the requirement for individualised pre- and post- test counselling should be commensurate with the predictive nature of the test, the sensitivity of the findings conferred by a test, and the range of clinical options available. There are numerous heritable characteristics that do not satisfy any of these criteria and therefore it would seem disproportionate to impose an obligation for mandatory pre- and post- test counselling. With respect to heritable disorders specifically, this may be particularly the case with carrier testing.

[4] Such as the following (accessed from 23andMe on 2nd December 2009):*The genetic information provided by 23andMe is for research and educational use only. . . . The Services Content is not to be, and is not intended to be, used for any diagnostic purpose and is not a substitute for professional medical advice. . . . [O]ur testing service is not licensed by the relevant state and federal authorities for genetic testing conducted for health and disease-related purposes.'*

[5] Zimmern RL & Kroese M. The evaluation of genetic tests. J Pub Health (2007) 29: 246

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Whilst the delivery of counselling as a necessary adjunct of genetic testing is well established in the context of health care delivery in many countries, we are aware that the requirement for pre- and post- test counselling could operate as a bar to offering genetic testing in some jurisdictions. Issues of distributive justice need to be balanced against concerns about the safety of individuals undergoing testing.

We also note that, in addition to providing extensive information of unknown medical benefit, genome-wide assays may provide information about heritable disorders without this necessarily being the core focus of the consumer. Therefore, whilst *availability of access* to pre- and post- test counselling from such services should form part of best practice, we do not believe that it should be required for all such tests.

2. **Do you believe there are certain genetic tests that should not be offered direct-to-consumers? If so, which categories of tests?**

   We agree with the approach that has been adopted – namely that no genetic tests should be expressly excluded from being made available direct-to-consumer, due to lack of evidence of direct harm resulting from such tests.

3. **Pre-symptomatic and susceptibility/pre-dispositional health tests are distinct categories in the draft of the Principles. Do you believe that this distinction is both valid and robust? If not, do you believe these two groups of tests could be stratified better?**

   Although we understand that the distinction between pre-symptomatic and susceptibility/ pre-dispositional health tests is neither scientifically valid nor clinically robust, we nevertheless believe that the distinction may be of value for guiding the provision of appropriate support. Our view is that the suggested figure of 5% penetrance as an appropriate threshold for pre-symptomatic tests is too low, and implies a level of statistical certainty which is not often found in many pre-symptomatic tests. We would prefer that test providers explicitly provide information on penetrance, or the amount of the overall variance of disease, explained by their test. In particular, services providers should make every effort to distinguish highly predictive tests for familial diseases from less predictive susceptibility tests for common diseases – for example, a clear distinction should be made between testing for mutations in the *presenilin* genes, which is highly predictive for familial early-onset Alzheimer's disease, versus testing for variants of the *APOE* gene, which has very low predictive ability for late-onset Alzheimer's disease.

4. **Should the Principles recommend that pharmocogenetic tests only be provided to consumers with individualised pre- and post-test counselling and should they fall into the bracket of 'genetic tests in the context of inherited or heritable disorders'?**

   We do not believe that pre- and post- test counselling should be required for pharmacogenetic testing, for several reasons: first, the information may only be relevant when taking the relevant drug, which will usually be under the supervision of a medical professional; second, many of the tests currently available do not have sufficient evidence of clinical validity or utility to warrant their implementation within healthcare systems and therefore should not be subject to medical regulation

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(see earlier); and third, the fact that such information is necessarily provided by genome-wide technologies does not imply that the individual consumer is either interested in, or likely to be harmed by, pharmacogenetic information.

5. **Are the impact criteria listed in Principle 10.1 (in addition to the categorisation of tests) a helpful additional way of stratifying genetic tests? Should a list of tests be included in the Principles that determine to which genetic tests the application of principle 10.1 is relevant?**

In principle, we feel that these lists are useful (though the list of tests currently misses out fetal sex determination) but note that, in many cases, a single provider will offer multiples of these tests within the same service. The lists may nonetheless be a useful aid for providers to consider the potential impact of results on consumers for different types of tests, and therefore to assess what types of professional support and expertise should be made available. However we do have some concerns that the process of establishing whether the test is likely to have a significant or detrimental impact on a potential consumer could be regarded as intrusive. There is a fine balance to be drawn between an obligation upon providers to protect potential consumers from harm, and paternalism. This is particularly the case for the last bullet point (namely the potential for the test to have a significant impact on personal relationships and the stability of the families).

6. **Are there any principles that are applicable to certain genetic tests that you consider should not be applied to that test? Specifically, do you consider the amount of information that test providers will be expected to provide to consumers to be excessive for some tests?**

We note that relevance of the first two bullets will vary according to test category, and suggest that it may not necessary to employ an appropriately qualified medical professional for the interpretation of all genetic tests (e.g. genealogy). There is a concern about the volume of information which might have to be provided and the means by which providers can be seen to have discharged their duties under principle 10. It would be helpful to have more discussion about the tools that could be employed to encourage consumers to read relevant test information. These could include timed screen shots, online tutorials, etc. Any of these tools should be balanced against the autonomous right of consumers to choose not to be informed of relevant information, but such methods could substantially improve public understanding and the ability of consumers to give informed consent.

7. **Should principle 5.10 be included? (Genetic testing of children)**

The requirement for a fully informed consent that is commensurate with the risks, benefits, limitations and implications of the test allows providers to seek a form of consent which is proportionate to the test purpose. However, principle 5.10 seems to have been framed with existing guidance from clinical genetics firmly in mind. Whilst it may be reasonable for tests to be delayed for diagnostic, pre-symptomatic and carrier tests conferring significant medical information, this cautious approach may not be appropriate for tests which involve acquisition of genetic information but are more recreational in nature (such as ancestry testing). To apply a moratorium against testing minors implies a degree of genetic exceptionalism which ignores the fact that there are many other ways that parents acquire knowledge of their children.

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However, we accept that the autonomy of future adult should be respected wherever possible, and that genetic tests including genome-wide assays have the potential to seriously undermine this right. We therefore agree with the inclusion of principle 5.10 and believe that test providers should be discouraged from testing children and making predictions about their 'inborn talents' or future health.

8. **Principle 5.3 states: "The test provider should take reasonable steps to assure themselves that a biological specimen provided for testing was obtained from the person identified as the sample provider. They should obtain a signed statement to this effect from the person buying the test". What do you consider to be 'reasonable steps' and should the Principles state what these steps should be?**

We agree that the test provider take reasonable steps to establish the provenance of the sample. The requirement for 'reasonableness' implies that this is proportionate obligation, suggesting that the provider could employ a variety of different strategies depending upon the application. This obligation is defensible because it is possible that samples could be sent for testing fraudulently, or without proper consent, and test providers need to take reasonable steps to ensure that the opportunity for fraud is minimised.

One difficulty is that the principles are intended to apply across jurisdictions and the framework document might contradict national legislation which would take precedence over voluntary guidance. For this reason it would be prudent for the principles to distinguish between statements of best practice and legal obligation[6].

We believe that the requirement for a signed statement is both reasonable and practical (at the point of testing), and would suggest that such a requirement could potentially be applied to all DTC *in vitro* tests based on human biological samples. The more rigorous requirement for the taking of samples to be witnessed by an independent third party is inappropriate in our view unless this is a statutory obligation (such as where samples are taken for paternity testing to support court orders imposing obligations for financial support within the UK). Again there needs to be a balance between preventing misuse or avoidable harms to consumers, and unnecessary intrusion.

9. **After discussions within the working group the following principle was not included: "A test provider must take whatever measures are necessary and appropriate to ensure that an individual has provided informed consent and has capacity to provide that consent for a genetic test." Do you think this principle should be or should not be included?**

We agree that this Principle should not be included. Our view is that placing such an obligation upon a test provider to ensure a valid consent from a competent consumer is either unenforceable, or would require such a potentially intrusive degree of enquiry of consumers, that the privacy of consumers might be breached. Arguably it is foreseeable that consumers could claim that their human rights had been breached if this obligation was included[7] (such as those under Article 8 which confer a right to respect for private and family life, home and correspondence). However, as mentioned above, there may be a variety of strategies which could place the onus upon the consumer to be truthful and be properly informed (such as a signed

[6] See for example, UK Human Tissue Authority (2007) Code of Practice 8: Import and export of human bodies, body parts and tissue, paragraph 23.
[7] UK Human Rights Act 1998.

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statement to this effect or timed provision of information to a prerequisite for providing the test).

10. Are any of the principles impossible to apply in your jurisdiction given existing national legislation or regulatory constraints?

We do not believe that any of the Principles would be impossible to apply within the UK. However, it should be noted that existing legislation, such as the UK Human Tissue legislation, is not enforceable in respect of paternity testing accessed from a provider outside the UK (although codes of practice purport to apply to this type of test).

11. Do you believe that test providers should sign up to the Principles and what costs do you expect will be incurred by complying with the Principles?

We believe that the costs will be small to moderate, but should not be prohibitive.

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