The past year has been marked by the emergence of several companies, such as 23andMe, deCODEME, Navigenics and Knome, offering tests using genome-wide technology direct to consumers over the internet. On the basis of the published research findings of GWAS and other studies, these companies will calculate an individual’s risk to a number of common diseases, without the necessity of going through a medical practitioner. One of the significant challenges of direct-to-consumer testing is that it shifts the control of genetic testing from the clinical domain and medical professionals into the hands of consumers. No longer is genetic testing being carried out solely for medical reasons, by specialists in clinical genetics. Testing is now being used to empower consumers and can be used ‘to shed new light on your distant ancestors, your close family and most of all, yourself’ (23andMe). Such information can be shared with family and friends for ‘fun’, as part of the new ‘recreational genomics’. Direct-to-consumer testing challenges many of the assumptions that underpin current practice surrounding genetic tests while at the same time exposing the deficiencies in the current regulatory frameworks to regulate this area. The purpose of this paper is to explore some of these issues, at a time when the science and the law are changing rapidly.

MARKETING STRATEGIES

Currently, the three main players that have received the most media coverage in this new global market are 23andMe, Navigenics (both based in CA, USA) and deCODEME (offices in Reykjavik, Iceland) (7). For a one-off payment of ~US$1000, 23andMe will genotype 580 000 SNPs in your genome (deCODEME 1 million for US$1000; Navigenics 1.8 million for $2500 plus $250 per year thereafter), so that “you can use our interactive tools to shed new light on your distant ancestors, your close family and most of all, yourself” (2). In interviews with journalists, co-founders Linda Avey and Anne Wojcicki stress that 23andMe will empower individuals, who can use the tools provided by 23andMe to determine ancestry; compare their DNA with findings from the scientific literature about disease susceptibility and genetic variation in different global populations; as well as share the information with other people as part of a social-networking tool, similar to Facebook (8). This focus on social-networking is echoed in the marketing strategy of deCODEME, which also allows people to share information to compare ancestry, a major past time in Iceland. The marketing strategy of Navigenics...
is slightly different, as they pitch their service as a way to access more information in order to plan your health strategy. ‘With this knowledge comes power. You can take appropriate action: setting your health priorities, taking prevention measures, becoming vigilant about early symptoms, or beginning treatment earlier, which can improve health outcomes’ (9). While Navigenics requires a one-off fee of $2500, the further $250 per year that is charged by Navigenics is to provide on-going information and access to genetic counsellors for consumers.

THE NATURE OF THE TESTS OFFERED

With their focus on social networking, one of the things that 23andMe will tell you is whether you have the genetic variation that makes brussel sprouts taste bitter to you. This interesting ‘fun’ fact you can share with your friends or biological relatives. At the same time, 23andMe, like other companies in this field, also test for more serious health-related conditions, although both kinds of tests are marketed in the same way (10). Consumers are given the results of a combination of tests for common conditions, which give an indication of an individual’s relative risk compared with someone of the same age, or gender, in the general population, and, for several companies, an estimate of absolute risk. These results could potentially be misleading as the estimated relative or absolute risks might be accurate on average, but very inaccurate for an individual. For example, a woman could have a low relative risk for breast cancer based on a genetic test of common variants. However, if she has two first-degree relatives who developed breast cancer before the age of 40, her absolute risk will be much higher than the average person with the same genotypes at those common variants. Unless this distinction is clearly understood, there is the possibility that consumers may develop a false sense of security about their genetic risk. Harm may occur if, in failing to understand the significance of the information that companies provide, individuals do not take preventative action or, on the other hand, worry unnecessarily about the significance of the results. Although Navigenics offer a genetic counselling service to help consumers understand the significance of the results provided, they also recommend that individuals take their test results to physicians to provide an analysis of the absolute risk to the individual. The onus is on the consumer to seek this advice. The marketing of direct-to-consumer tests as a social networking facility also creates the possibility that people may share these results, while being unaware of their true statistical significance, which could lead to unintended consequences and possible harms.

DISCLAIMERS

In recognition of the limitations of the risk information that they can provide, each company has substantial disclaimers in the online information form that consumers must read before they are sent a buccal swab or spit vessel. This performs the dual function of informing consumers but also protecting the companies from liability. Each company is very keen to ensure that the information provided to consumers is ‘not intended to substitute for professional medical advice, diagnosis or treatment’ (11). For example, 23andMe requires that customers ‘understand that information you learn from 23andMe is not designed to diagnose, prevent or treat any condition or disease or to ascertain the state of your health and that you understand that 23andMe’s services are intended for educational, informational and research purposes only (12). deCODEME also makes consumers aware that the ‘risk estimates are only as accurate as the data used in the risk model. You acknowledge your understanding of genetic risk as a statistical measure that has implications derived from a large group of people with characteristics equivalent to yours but does not determine your chances for getting the corresponding disease, the disease severity or the disease outcome’ (13). These disclaimers acknowledge the current lack of sensitivity and the poor predictive value of such tests (14), which is a responsible thing to do, but must leave the consumer wondering exactly what they are paying for (15).

For these reasons, in current research practice, individual results of GWAS are not reported back to individuals, because at this stage findings can be difficult to interpret and are not clinically relevant. However, the large amount of information provided by GWAS can still provide ethical dilemmas. For example, there may be incidental findings that may have significance for individuals, which are found as a result of the extensive genome scanning that is carried out, and may be generally known to those medically trained, or working in a particular disease area, as constituting a significant risk. In such circumstances, researchers may be placed in the difficult position of having to decide whether the condition is of significant danger to the individual and is treatable, and therefore would warrant re-identification and contact with the research participant in order to warn them. Although such situations are challenging in the research context and good practice is still evolving, there are support mechanisms and decision-making structures to deal with such circumstances. In the case of direct-to-consumer testing, all significant findings based on GWAS analysis and current scientific knowledge will be reported back to the consumer.

THE CHANGE IN SERVICE DELIVERY

These marketing strategies target healthy individuals who may not have sought help through the health services, rather than patients, or people who may already have a family history of disease. Therefore, direct-to-consumer services have the potential to transform the way that genetic testing is currently offered and managed, as companies offer an alternative to going through the conventional route of the health service to seek personal genetic information (16). Current best clinical practice would require that the results of a genetic test be conveyed by a specialist clinical geneticist or genetic counsellor, using their specialist knowledge to interpret the results specifically for the individual. These procedures have been developed for monogenic conditions rather than common diseases, on the basis that the interpretation of results can be sometimes be complex and will vary between individuals with different family histories. These safeguards have been developed because of the significant implications that some
genetic tests will have for other family members, as well as the individual’s health, lifestyle, insurance and employment prospects. Although service provision has been designed largely with monogenic disease in mind, the concerns about the use of information and the possible harms from misuse of this information can be the same for common diseases.

All of the direct-to-consumer companies surveyed, actively encourage consumers ‘to seek the advice of health professionals if you have questions or concerns arising from your genetic information’ (12). Only Navigenics offers a genetic counselling service to subscribers, to help them understand the significance of their results, but they also recommend seeking specialist advice. The separation of information-giving from clinical interpretation has a number of implications. As Hunter et al. (14) suggest it could result in an extra burden falling on health services, as ‘consumers enter the surgeries of ill-prepared doctors, with a genome map and printouts of risk estimates in hand’ (14). Others argue that direct-to-consumer tests could potentially allow individuals to take greater responsibility for safeguarding their own health and result in the democratization of medicine (17). In addition, the provision of genetic counselling services by companies may buttress the health services, which in the UK are poorly equipped to deal with genetic services for common diseases. Such counselling may also go some way to ensuring that consumers do not stop treatment prescribed by a doctor, or seek new unnecessary treatment based on their own interpretation of their test results. An additional concern is whether it is fair for national health services to have to provide interpretative, professional services for ‘worried’ patients who have been given results by companies that are located in other countries (15).

THE LACK OF EFFECTIVE REGULATORY CONTROLS

The reason that such companies can market GWA tests in such a way is that there are few regulatory controls in place at national, European or global levels to first assess the clinical validity of tests before they get to market or, secondly, to control marketing to the public (18). This is partly due to the fact that the use of genetic tests for diagnosis, treatment and determining carrier status is still in its infancy, with most tests being offered in Europe through the national health services (with the exception of Germany). One of the problems has been that genetic tests within the European Union were not subject to independent pre-market review, as they are considered ‘low risk’ (19) under the In Vitro Medical Devices Directive (20). The latest development within Europe is the Additional Protocol on Genetic Testing, which has just been passed by the Council of Ministers of the Council of Europe (21). This will be the first European legal instrument in this area and will be open for signing in November 2008. It will apply to all genetic tests whether they are provided publicly or privately and it requires that the clinical utility of a genetic test must be determined before deciding to offer this test to a person or a group of persons (22), as well as that all genetic testing must be accompanied by genetic counselling that is appropriate to the individual (23). This could have significant implications for certain direct-to-consumer tests, if it is widely adopted within Europe (24).

In the USA, the lack of an appropriate regulatory system is also evident and although commercial companies offering genetic tests are on the increase, ‘there is no mechanism to ensure that genetic tests are supported by adequate evidence before they are marketed or that marketing claims for such tests are truthful and not misleading’ (25). The FDA does not require that the test have any clinical application—just that it can do what it says that it will do. For example, the Roche Amplichip was passed even though it does not refer to a specific drug, but just that the CYP2D6 and CYP2C19 genotypes ‘may be used as an aid to clinicians in determining therapeutic strategy and treatment dose for therapeutics that are metabolized by these genes’ (25).

Even though an appropriate regulatory system does not exist at a Federal level, state bodies in California and New York are taking action against direct-to-consumer, genetic-testing companies. In June 2008, the California state government issued ‘cease-and-desist’ letters to 13 companies demanding they immediately stop selling genetic tests to California residents. The letters required that the companies provided evidence that their laboratories were properly licensed and certified, and that all tests were requested by physicians (26). This action by the state authorities raises a number of key issues. These are: whether there is a significant difference between a genetic risk assessment and a diagnostic test to warrant different regulation; what tests should under the control of medical professionals; should consumers be able to access their own DNA data without restriction; and what the role of the state should be in regulating genetic tests. Ryan Phelan, chief executive of DNA Direct, welcomes regulation of direct-to-consumer testing and calls for ‘nuanced regulation’ that distinguishes between tests predicting serious diseases and those revealing interesting, fun information unrelated to health (26). The unfolding events in the USA, will be a test case for direct-to-consumer testing, and will determine how national law enforcement bodies can influence the activities of companies based outside of their jurisdiction.

Direct-to-consumer testing challenges many of the practices that have been developed around genetic testing and highlights the gaps in the regulatory regimes when applied to commercial testing of this kind. One of the significant challenges of direct-to-consumer testing is that it shifts the control of genetic testing from the clinical domain and medical professionals into the hands of consumers. No longer is genetic testing being carried out solely for medical reasons, by specialists in clinical genetics. This shift in control from the medical profession has caused consternation, but may force a re-evaluation of the way genetic testing is currently carried out and in the long term lead to better services driven by consumer needs. Currently, companies providing direct-to-consumer tests do not provide the same quality of advice and information specific to an individual’s circumstances that is offered by health services. The new European Additional Protocol on Genetic Testing and the stance by authorities in California and New York suggest that the involvement of medical professionals in the prescribing and interpretation of genetic tests is regarded as necessary.
It remains to be seen how events will play out and if additional mechanisms will be put in place to regulate direct-to-consumer testing over the coming year.

ACKNOWLEDGEMENTS
Thanks to the Oxford Bioethics Network GWAS discussion group for providing insights into some of these issues.

Conflict of Interest statement. None declared.

FUNDING
Funding for this work was provided by the Wellcome Trust Biomedical Ethics programme.

REFERENCES
2. https://www.23andme.com/ (accessed 03/07/08)
6. In addition, there are companies that offer other kinds of tests such as using DNA to identify ancestry (Genetrack Biolabs http://www.dnaancestrynproject.co; DNA Print Genomics http://www.danaprint.com; IBM/National Genographic Project http://tinyurl.com/34lygbu); for personalised diet, lifestyle and nutrition (MycellF www.sciona.com; Salugen http://www.salugen.com); individual responses to nicotine (G-nostics http://www.nicotest.com) and a dating service based on genes associated with the immune system (ScientificMatch.com http://www.scientificmatch.com); as well as testing for common diseases (DNATraits http://www.dnatraits.com/index.php/catalog).
7. Knome offers a whole genome scan for US$350,000, which places them out of the reach of the vast majority of consumers. Another company offering a similar service is DNA Direct http://www.dnadiirect.com/.
8. http://www.youtube.com/watch?v=F7UH0BHbhho (accessed 03/07/08)
11. https://www.navigenics.com/ (accessed 30/06/08)
12. https://www.23andme.com/about/consent/ (accessed 30/06/08)
13. In the information form for people registering to the site http://www.decodeme.com/ (accessed 03/07/08)
18. While there are documents such as the OECD Guidelines for Quality Assurance in Molecular Genetic Testing 2007 that provide principles for policy guidance, much of the regulation is carried out at a national level.
24. This Additional Protocol will only affect countries that have signed the Council of Europe Convention on Human Rights and Biomedicine 1997 ETS No. 164, of which a number of key countries within the Europe, such as the UK has not signed. Even for signatories of the Convention, it is still an optional protocol and will have to be implemented into national law to have full effect.