# Horizon Scanning Series
# The Future of Precision Medicine in Australia

## *Legal and Regulatory Issues of Precision Medicine*

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# Legal and Regulatory Issues

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## 1. Public trust and the law

In any democratic society, the legal system is charged with maintaining the fundamental rights and freedoms to which that society ascribes value. However, in no society are the rights and freedoms of individuals absolute. The challenge for law-makers is to ensure that the exercise of each individual's rights and freedoms interfere to the least extent possible with those of others and that, in attempting to achieve an appropriate balance, the law itself does not become an unreasonable fetter on their exercise.

In times of rapid technological change, there is a risk that old laws created for particular purposes could act as barriers to the enjoyment of new or enhanced rights and freedoms brought about by new innovations. But there is an equal risk that society will suffer if these innovations proceed unfettered by the law, given the vital role that the law plays in protecting individuals in accordance with the rights and freedoms that society holds dear. Many legal scholars are exploring these issues. One exampleis Graeme Laurie (2017), who, with his research team is identifying what he refers to as 'regulatory congestions' and 'regulatory gaps' in his Liminal Spaces Project (2017).

In the context of precision medicine, the challenge for the Australian legal system is to provide an appropriate regulatory framework to facilitate access to new technological developments in ways that respect the rights and freedoms of individuals and the broader values of society as a whole. This requires a legal system that not only promotes safe, efficient, effective and equitable access to the technology, but also reflects societal attitudes towards that technology. To achieve this end, the Australian legal system should be uniform across all of the states and territories, and should also be harmonised, to the greatest extent possible, with the legal systems of other countries, so that Australian citizens get the same benefits from precision medicine as do the citizens of other countries.

There will be some instances where, no matter how innovative a technology might be, it will not be acceptable to contemporary society. Two such examples are reproductive cloning and germline gene therapy. Australian society has chosen, through its legislators, to absolutely prohibit these interventions through the *Prohibition of Human Cloning for Reproduction Act 2002* (Cth). One incidental consequence of this prohibitory legislation, however, is that other, newer technological advances are, or may be prohibited. For example, some aspects of mitochondrial replacement therapy and genome editing research using human embryos may not be allowed to be performed in Australia (Whitton et al in press). One consequence is it may not be possible in Australia to undertake the types of CRISPR-mediated gene editing research undertaken on human embryos and zyogotes by Ma et al (2017) in the United States and Tang et al (2017) and other research teams in China. It shoud be noted that the *Research involving Embryos Act 2002* (Cth) also has relevant provisions in this regard (Whitton et al in press).

Laws, of their nature, tend to be blunt and inflexible instruments. Unless they have built in review mechanisms or sunset clauses, laws in this area need to be regularly revisited and updated, to ensure they continue to reflect societal values and, equally importantly, that they provide clarity as to the obligations they create in all areas of technology.

The assessment of societal responses to new technological developments has both normative and

practical aspects. Ethical principles such autonomy, beneficence, justice and solidarity are vital touchstones in determining what is acceptable to society. But we also need to understand more practically how contemporary society views technology: what is viewed as acceptable and what is not. The law must be guided as much by these norms and views of society towards new technologies as it is by the technology itself. Public trust is vital. As Chalmers and Nicol (2004) suggest, '[u]nless there is public trust in the scientists undertaking this research and the regulatory agencies charged with overseeing their work, the promise of the biotechnology revolution may never be realised'.

Scientists and technologists should not fear judgement by society. Australian and international research shows that people in democratic countries have confidence in science, particularly biomedical science. Research by scholars such as Bruce and Critchley (2008-2015), Henneman et al (2008) Gaskell et al (2000) and others (reviewed in Critchley & Nicol in press) has consistently found that Australians, Europeans and North Americans are generally positive about genomic research if it is directed towards discoveries that have beneficial applications that are in their interest. In the context of precision medicine, then, the key legal challenge is how to effectively facilitate and regulate its practice, so that we maximize the potential benefits, while avoiding harms to society and wasted resources. Nicol et al (2015) identify five key recurring elements that must be taken into account in assessing the adequacy of the legal regulation of precision medicine and the need for law reform:

1. appropriate consideration of safety, efficacy, and patient need;
2. cost effectiveness;
3. consistency/equivalency across geographical, technological, and institutional borders;
4. respect for cultural differences; and
5. genuine engagement with all relevant stakeholders.

## 2. Privacy

Health information has long been seen to raise particular privacy concerns because of its deeply personal and sensitive nature. As noted by Otlowski and Eckstein (in press), genetic information raises additional privacy concerns because it can be both diagnostic and predictive, both personal and familial, both highly relevant and irrelevant to third parties, and of both immediate and future relevance to individuals. Because of the particular characteristics of genetic data, even when de-identified, it is always inherently identifiable, so special protections are required, especially if such data is to be linked to other sensitive information (Chalmers, Nicol & Otlowski 2014). Processes for protecting the privacy of data are constantly evolving. As mechanisms for data protection become increasingly sophisticated, new strategies emerge to outflank protections (Erlich & Narayanan 2014; Gymrek et al 2013.) The reality is that once data is released into the public domain, neither participants nor researchers can control its use, or the possibility of that data being linked to other data sets (Kaye et al 2009). The challenge for researchers charged with protecting the privacy of genetic information is reflected in Chapter 3.2 of the NHMRC National Statement on Ethical Conduct in Human Research, which states: 'With advances in genetic knowledge and data linkage, and the proliferation of tissue banks of identified material, human tissue samples should always be regarded as, in principle, re-identifiable.'

The legislative regime for the protection of privacy is particularly complex in Australia because of our federal system of government and the limitations on federal legislative power imposed by the Constitution. As a result, there are both federal and state-based privacy statutes. State-based laws govern the privacy of information held by state government agencies, which include public hospitals and many universities. The federal *Privacy Act 1988* (Cth) (*Privacy Act*), in contrast, governs federal government agencies and corporations, subject to certain exceptions. To add a further layer of complication, until 2014 different obligations were imposed on federal government agencies, through a set of Information Privacy Principles, and corporations, through the National Privacy Principles. The *Privacy Amendment (Enhancing Privacy Protection) Act 2012* (Cth) created a new uniform set of

Australian Privacy Principles (APPs). Primarily, the APPs create obligations relating to the collection, storage, use and dissemination of, and provision of access to personal information.

In 2002-2003, the Australian Law Reform Commission (ALRC) and Australian Health Ethics Committee (AHEC) were jointly tasked with conducting a public inquiry into the protection of genetic information in Australia. The final report of the ALRC/AHEC inquiry, *Essentially Yours* (2003), emphatically rejected any notion of genetic exceptionalism (that genetic information should be seen as uniquely powerful and calling for unique solutions). However, the special status of genetic information and the need for enhanced protection in some areas was recognised in the Report, and various recommendations were made, including amendments to the *Privacy Act*. As explained by Otlowski and Nicol (2013), many of these recommendations have been implemented, including the inclusion in the *Privacy Act* of a definition of genetic information as information 'about an individual in a form that is, or could be, predictive of the health of the individual or a genetic relative of the individual' amongst other things. Health information is a form of 'sensitive information' which is given enhanced protection under the Act, as is genetic information about an individual that is not otherwise health information.

There are, nevertheless, ongoing deficiencies in Australian privacy laws, not least of which is the lack of national consistency. Another problem is that the current federal regime is focussed on the protection of information and records. Otlowski (2013) explains that genetic samples are currently not protected, notwithstanding that such samples potentially hold a substantial amount of information about the individual concerned. Additionally, enforcement mechanisms available under this regime are weak and what protections that do exist are lost once information is outside jurisdictional boundaries.

One issue that has been addressed is sharing of information with family members at risk. In 2014 guidelines were introduced to regulate the disclosure of relevant genetic information to genetic relatives, notwithstanding the lack of consent from the index patient (NHMRC 2014a). These guidelines do not create a *duty* to disclose relevant information to a genetic relative without the consent of the patient; rather, they provide protection from such disclosure breaching the *Privacy Act,* provided that the guidelines have been closely followed. Although representing an important step forward, they still fall short of comprehensive coverage as they do not cover health practitioners working in state-based public hospitals. As Otlowski (2015) notes, to date, only New South Wales has introduced equivalent state legislation through the *Health Legislation Amendment Act 2012* (NSW), amending the NSW Health Privacy Principles to make them consistent with the federal guidelines.

Although not strictly privacy issues, other emerging areas of concern arising from the increased availability of next generation sequencing are return of results of genomic analyses and disclosure of incidental findings to a research participant or patient who may have requested not to be informed, or may have only given limited consent, in the sense that the issues that have come to the fore were not in the contemplation of either of the parties when consent was given. Privacy laws give individuals the right to know what information is being held about them. In the context of genomics, in particular, the right not to know is increasingly being seen as important as the right to know. There is not as yet any resolution to the question of whether this right not to know can or should be enshrined in law.

Looking to the future, the Australian federal parliament is currently considering whether to approve an amendment to privacy legislation that would make it a criminal offence to re-identify de-identified government data. Whilst not directly relevant to personal genetic data, this illustrates the seriousness with which the federal government views the protection of privacy.

## 3. Insurance

Concerns about discrimination on the basis of genetic information have been raised for some years and, now, with next generation sequencing, and the proliferation of genetic information, the risk of

such discrimination has been heightened. Life insurance has been the main focus of these concerns in Australia as, unlike health insurance which is community rated, life insurance is based on individual risk assessment and applicants for life insurance are required to disclose all relevant health information including the results of any genetic tests undertaken. Due to the exemption that life insurers have under the *Disability Discrimination Act 1992 (Cth)* s 46*,* they may take genetic test results into account when underwriting for life insurance, provided that they can substantiate their decisions on actuarial, statistical or other reasonable grounds. This includes not only genetic testing undertaken for clinical purposes but also genetic results obtained in the course of participation in research, notwithstanding the fact that such results are typically not undertaken in accrediated testing laboratories.

Whilst this does, in theory, provide protection to individuals from unfair discrimination, in practice, it is difficult for applicants to know the reasons for a decision and the onus is on the applicant to challenge the decision, which can be a time consuming and expensive, particularly if it involves legal proceedings against the insurer. The ALRC/AHEC *Essentially Yours* Report (2003) had recommended greater protections for consumers, including a process for vetting which genetic tests were suitable for insurance underwriting. However, these key recommendations were left to the life insurance industry to implement and there has been negligible follow up. Keogh and colleagues (2009; 2017) provide useful reviews of the growing calls in Australia to restrict life insurers access to genetic test information, particularly as evidence comes to light that the *fear* of genetic discrimination is negatively impacting on the update of genetic testing and the willingness of people to participate in genetic research.

The laissez-faire stance taken in Australia, leaving it to life insurers to self-regulate, is in marked contrast to the position in many European countries which have legislated to prohibit life insurers from using genetic test information (Otlowski et al 2012). In the UK, a moratorium on the use of genetic test information by insurers has been in place since 2001. Canada has also recently introduced legislation (the *Genetic Non-Discrimination Act 2017*) prohibiting life insurers from using genetic test results for underwriting purposes. A current Australian Parliamentary Joint Committee inquiry into Corporations and Financial Services (2017) has received submissions in relation to the problem of genetic discrimination and is due to report later this year and may well call for similar reform in Australia.

Inevitably, it comes down to a balancing of interests: on the one hand, the interests of patients/research participants/consumers and on the other, the interests of life insurers and maintaining the viability of the life insurance industry. The fear of 'adverse selection' is cited as the major factor justifying life insurers accessing genetic test information. In particular the concern is that individuals who have undertaken genetic testing and established that they are at higher risk of future disease will apply for large policies and those who are low risk may not take out life insurance at all, thereby distorting the pool of insureds (Harper 1997). It is argued on behalf of the industry that restricting their access to genetic test information will undermine their ability to effectively underwrite and thereby threatens the viability of the industry. However, the experience in the UK where a moratorium prevails and in many European countries, which have prohibited insurers' use of genetic test information in life insurance underwriting does not bear out the drastic consequences suggested. Expsoure to adverse selection is more likely to arise from tests for single gene disorders rather than for complex diseases, and these currently remain relatively rare (Macdonald 2011). Expert actuarial reports indicate that for the time being, where a relatively small proportion of the population has undergone genetic testing, the impact on the life insurance market of a ban is not likely to be significant (Macdonald 2011; Hoy and Durnin 2012.) They do note that this may change over time as genetic testing becomes more common-place, and that different approaches to life insurance may be required in the future to deal with this.

## 4. Safety and regulation

Whilst precision medicine might be scientifically new, it exists within well-established regulatory and oversight systems aimed at protecting the safety and wellbeing of individuals, irrespective of whether they might be described as patients, research participants or consumers. Included in this body of regulatory instruments are generalist consumer protection and tort laws, specific health-related laws and even more highly specific laws targeted to genomics and related technologies. This complex and intersecting body of laws has been described by Nicol et al (2016) as a 'regulatory soup'. Some examples of the challenges to existing regulatory schemes brought about by precision medicine are highlighted below.

The *Therapeutic Goods Act 1989* (Cth) plays a crucial role in regulating the supply of health-related products in Australia. The Act is administered by the Therapeutic Goods Administration (TGA), and regulates the introduction of therapeutic goods into the Australian market. Drugs must satisfy rigorous pre-market assessment standards prior to marketing approval, requiring evidence of clinical utility, safety and efficacy through clinical trials approved and monitored by Human Research Ethics Committees (HRECs). Fast track registration may be allowed in limited circumstances where there is unmet clinical need. Precision medicine is creating a number of challenges to this well-established system for drug approvals. For instance, the requirement for phase 3 randomised double blinded clinical trials is problematic for personalised therapies, the effectiveness of which cannot be evidenced statistically across a population. Some of the exemptions from regulatory approval also need to be revisited in the context of precision medicine. One example is the exclusion of human tissues and cells collected from patients and returned to them after *ex vivo* treatment. McLean et al (2015) point out that this exclusion, perhaps inappropriately, extends to autologous stem cell products.

For devices, including diagnostic genetic tests, which are classified as in vitro devices (IVDs), the stringency of pre-market assessment depends on risk classification. It is prohibited in Australia to make available to individuals genetic test kits for self-testing for the presence of or susceptibility to serious diseases. In contrast, genetic test kits used in the laboratory, as well as laboratory-developed tests can be approved by the TGA provided that they comply with essential principles relating to quality, safety and performance. However, foreign providers of genetic tests who make their services available directly to consumers through the internet are not regulated through this legislation. As argued by Nicol and Hagger (2013), further work needs to be done to explore regulatory options and to improve consumer understanding of genetic testing. In order to help address these issues, the NHMRC has produced an information resource for consumers (2014c) as well as more general statement cautioning about the use of direct to consumer genetic testing (2014d).

Genome editing research using human embryos comes within the ambit of the *Prohibition of Human Cloning for Reproduction Act 2002* (Cth) and the *Research Involving Human Embryos Act 2002* (Cth), administered by the NHMRC Embryo Research Licensing Committee, as well as the *Gene Technology Act 2000* (Cth), administered by the Office of the Gene Technology Regulator (OGTR). The *National Statement on Ethical Conduct in Human Research* also applies. There are a number of definitional issues and overlapping obligations with these regulatory frameworks in the context of precision medicine, and a lack of central coordination. It has been argued by Eckstein (2015) that the OGTR would be the appropriate regulator in the broader context of innovative genomic therapies, on the basis that the Office is 'well placed' to meet many of the challenges associated with risk-benefit assessment in the novel science space.

There can be little doubt that it would be beneficial to society to clear the 'regulatory soup' (Nicol et al 2016) and to ensure that the regulatory requirements for precision medicine are efficient, effective and transparent. Each new technological development poses new legal challenges. We are in a phase of considerable uncertainty at present, which is unlikely to change any time soon. We must be constantly vigilant in ensuring that our laws achieve the purpose that society expects of them.

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