Journal of Law and the Biosciences, 680–686
doi:10.1093/jlb/lsw053
Advance Access Publication 22 November 2016
Peer Commentary

Modernizing biomedical regulation: foresight and values in the promotion of responsible research and innovation

Shawn H.E. Harmon

Department of Law, University of Edinburgh School of Law, Edinburgh EH8 9YL, UK
Corresponding author: E-mail: Shawn.Harmon@ed.ac.uk

INTRODUCTION

A new, more responsive and personalized era in healthcare has long been anticipated.[1] And while one might dismiss as hyperbole some of the claims that have been made in relation 'personalized', 'stratified', or 'precision' medicine, it is undeniable that some of the associated technologies and practices (such as stem cell research, genome sequencing, and sample/data banking) do indeed promise to improve healthcare interventions, both preventive and curative.[2] This promise has given rise to widespread excitement, and to initiatives like US President Obama's *Precision Medicine Initiative*. Underwritten by US$215 million, it is meant to pioneer a model of patient-powered research that will result in new clinical knowledge and tools.[3] However, as Nicol et al. acknowledge (pp. 4–5) in their wide-ranging and informative article,[4] so-called precision medicine could also generate as much burden as boon.

1 Werner Kalow, *Pharmacogenetics and Personalised Medicine*, 16 FUND. & CLIN. PHARMACOL. 337 (2002); Andrew Miles & Michael Loughlin, *Evidence-based Healthcare, Clinical Knowledge and the Rise of Personalised Medicine*, 14 J. EVAL. CLIN. PRAC. 621 (2008).

2 See Robert S. Schwartz, *The Politics and Promise of Stem-Cell Research*, 355 NEW ENG. J. MED. 1189 (2006); Flora M. Vaccarino et al., *Annual Research Review: The Promise of Stem Cell Research for Neuropsychiatric Disorders*, 52 J. CHILD PSYCHOL. & PSYCHIATRY 504 (2011); Barbara R. Jasny, *Realities of Data Sharing Using the Genome Wars as a Case Study—an Historical Perspective and Commentary*, 2 EPJ DATA SCI. 1 (2013); Wei-Qi Wei & Joshua C. Denny, *Extracting Research-quality Phenotypes from Electronic Health Records To Support Precision Medicine*, 7GENOME MED. 1 (2015); Gert-Jan B. van Ommen et al., *BBMRI-ERIC as a Resource for Pharmaceutical and Life Science Industries: the Development of Biobank-based Expert Centres*, 23 EUR. J HUM. GENET. 893 (2015).

3 Jocelyn Kaiser, *Obama gives East Room Rollout to Precision Medicine Initiative*, http://www.sciencemag.org/news/2015/01/obama-gives-east-room-rollout-precision-medicine-initiative; White House, *Fact Sheet: President Obama's Precision Medicine Initiative*, at https://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative (both accessed Sept. 1, 2016).

4 Dianne Nicol et al., *Precision Medicine: Drowning in a Regulatory Soup?*, 3 J. L. & BIOSCI. 281 (2016).

For example, it could blur the boundaries between lab, clinic, innovation industries, and healthcare services, thereby inappropriately shifting research targets and measures of success; recreate the discourse patterns of other emerging technologies and practices, prompting speculative ethics, thereby squandering valuable ethical resources;[5] undermine existing regulatory structures aimed at key social (eg respect) and clinical (eg safety, efficacy) objectives, thereby weakening measures meant to ensure benefit; and contribute to regulatory construction, and so to overlap, confusion, and burden, thereby stifling innovation and promise.[6] And if our technical vision is achieved, it could exacerbate existing disparities in healthcare, both domestically and internationally, thereby moving us farther away from justice in health.

With respect to large-scale biobanking and data sharing, Nicol et al. correctly state that regulatory problems have been multiple, with consent looming large as an issue of concern.[7] Given that biobanks are part of a new research model that does not permit the effective functioning of traditional consent,[8] they have been met with significant ethical concern and regulatory construction, the result being a wave of policy statements, and normative claim making and standard setting.[9] Citing Collins and Varmus,[10] Nicol et al. state (p. 19), again correctly, that regulation must ensure that innovations are timely, widely affordable, safe, and effective. I contend that the notion of 'responsible research and innovation' (RRI) could contribute to these objectives, and, if used in combination with 'legal foresighting' (LF), could generate the evidence that is necessary to encourage better regulation (and decision making). Here, I briefly outline RRI and LF, arguing that they ought to facilitate the design of value-based regulation that is more 'future proof' than many examples on which we currently rely.

RRI AND LF

RRI is a broad and imprecise concept that has gained particular policy traction in Europe.[11] The notion of RRI grew out of earlier and ongoing discussions about research integrity relating to controversial technologies such as genomics, synthetic biology, and nanotechnologies,[12] as well as concerns about the value of science,[13] technology control in contexts of uncertainty and ignorance,[14] and the impact of globalism

---

5 For more on this, see Alfred Nordmann, *If and Then: A Critique of Speculative NanoEthics*, 1 NANOETHICS 31 (2007), and Alfred Nordmann & Arie Rip, *Mind the Gap Revisited*, 4 NAT. NANOTECH. 273 (2009).

6 In an informative paper reminiscent of Timothy Caulfield et al., *The Stem Cell Research Environment: A Patchwork of Patchworks*, 5 STEM CELL REV. REP. 82 (2009), to which both Bubela and this author contributed.

7 Zubin Master et al., *Biobanks, Consent and Claims of Consensus*, 9 NAT. METHODS 885 (2012).

8 Shawn H. E. Harmon, *Semantic, Pedantic or Paradigm Shift? Recruitment, Retention and Property in Modern Population Biobanking*, 16 EUR. J. HEALTH L. 27 (2008).

9 For a list, see Christopher Thomas Scott et al., *Personal Medicine—The New Banking Crisis*, 30 NAT. BIOTECH. 141 (2012), at Table 3.

10 Francis S. Collins & Harold Varmus, *A New Initiative on Precision Medicine*, 372 NEW ENG. J MED. 793 (2015).

11 European Commission, *Establishing Horizon 2020—The Framework Programme for Research and Innovation (2014–2020)*, COM(2011) 809 Final; European Commission, *Horizon 2020 Work Programme 2014-2015: Science with and for Society (Revised)*, EC Decision C(2015) 2453.

12 Barbara Adam & Chris Groves, *Futures Tended: Care and Future-Oriented Responsibility*, 31 BULL SCI. TECH & SOC. 17 (2011); RENÉ VON SCHOMBERG (ed.), TOWARD RESPONSIBLE RESEARCH AND INNOVATION IN THE ICTS AND SECURITIES TECHNOLOGIES FIELDS (2011).

13 MATTHEW KEARNES & MATTHIAS WEINROTH, A NEW MANDATE? RESEARCH POLICY IN A TECHNOLOGICAL SOCIETY (2011).

14 DAVID COLLINGRIDGE, THE SOCIAL CONTROL OF TECHNOLOGY (1980).

(Wright et al., 2011),[15] and ambitions to prevent technological disasters such as have been suffered in the past (Sutcliffe, 2011).[16] Informed by broad imperatives around caring and responsibility, RRI underwrites a regulatory framework comprised of 'anticipation', 'reflection', 'deliberation', and 'responsiveness'.[17] A central ambition is the fostering of integrated and representative mechanisms for continuous engagement around research and its governance;[18] it is claimed that RRI:

> … compels us to reflect on what sort of future(s) we want science and technology to bring into the world, what futures we care about, what challenges we want these to meet, what values these are anchored in, and whether the negotiations of such technologically-enabled futures are democratic. It asks how the targets for innovation can be identified in an ethical, inclusive, and equitable manner.[19]

RRI has therefore been associated with calls for processes supportive of taking broader views of science, of instigating culture-change therein, and of forming collective imaginaries that begin from much wider frames than are currently permitted in reflective practices.[20] In other words, scenario building and other reflexive exercises must allow actors to think more deeply not only about potential products and outcomes, but also about the purpose of science and innovation, and how to achieve the correct impacts from innovation.

Importantly, research has resulted in a framework that might be used to think more critically about *regulatory* possibilities in settings characterized by uncertainty; the notion (and practice) of LF is meant to generate diverse evidence supportive of more effective and durable governance practices and instruments.[21] It draws inspiration from the conviction, expressed 20 years ago, that stunning achievements in life sciences necessitate 'lengthened foresight', not only because of the consequences they can have for future generations, but also because of the non-traditional forms of oppression

---

[15] David Wright et al., *Precaution and Privacy Impact Assessment as Modes towards Risk Governance*, in Von Schomberg, *supra* note 12, 83–97.

[16] Hilary Sutcliffe, A Report on Responsible Research and Innovation, https://ec.europa.eu/research/science-society/document_library/pdf_06/rri-report-hilary-sutcliffe_en.pdf (accessed Aug. 25, 2016).

[17] Richard Owen & Nicola Goldberg, *Responsible Innovation: A Pilot Study with the UK Engineering and Physical Sciences Research Council*, 30 Risk Analysis 1699 (2010); Richard Owen et al., *A Framework for Responsible Innovation*, in Responsible Innovation: Managing The Responsible Emergence Of Science And Innovation In Society (Richard Owen, John Bessant & Maggy Heintz eds., 2013).

[18] Richard Owen, Phil Macnaghten & Jack Stilgoe, *Responsible Research and Innovation: From Science in Society to Science for Society, with Society*, 39 Sci. & Pub. Pol'y. 751 (2012); Bernd C. Stahl, *Responsible Research and Innovation: The Role of Privacy in an Emerging Framework*, 40 Sci. & Pub. Pol'y. 708 (2013).

[19] Owen et al., *supra* note 17, at 34–35.

[20] *Id.* and see Rob Bellamy, Jason Chilvers & Naomi E. Vaughan, *Deliberative Mapping of options for Tackling Climate Change: Citizens and Specialists 'Open Up' Appraisal of Geoengineering*, 25 Pub. Underst. Sci. 269 (2016).

[21] See Graeme Laurie, Shawn H. E. Harmon & Fabiana Arzuaga, *Foresighting Futures: Law, New Technologies and the Challenges of Regulating for Uncertainty*, 4 L. Innovation & Tech. 1 (2012), as refined in Shawn H. E. Harmon, 'Regulating New Technologies: A Case Study of Legal Foresighting', presented at 2014 Joint 4S/ESOCITE Meeting, Buenos Aires, Aug. 22, 2014, Shawn H. E. Harmon, 'Foresighting Futures', presented at Schulich School of Law Staff Seminar Series, Mar. 10, 2016, and Shawn H. E. Harmon, 'Evidence, Engagement and Transparency in Decision-Making', presented at Canadian Centre for Vaccinology, June 10,2016.

permitted by them (ie stemming from biological potentialities and relating to the often invisible distribution of life opportunities).[22] At base, LF is conceived as a future-oriented process aimed at identifying and exploring possible and desirable *legal or quasi-legal* interventions directed at better achieving valued social and technological ends; it is concerned with how to improve the process of designing governance systems so that they might more effectively use regulation to achieve socially justified public goods.[23]

The premises underlying LF are that, if we wish to better govern and operate in fluid and unstable settings (such as precision medicine), then we must:

1. accept that the law, though often limited and blunt, *may* properly play a significant role in articulating socio-technological objectives, in shaping behavior, and in measuring (and rectifying) the justness of outcomes, and *can and should* be more proactive and integral to the formation of new pathways of action;
2. reject the notion that past or existing uses of law represent good models, and be prepared to undertake a fundamental revisioning of the legal setting, its institutions, instruments, and mechanisms; and
3. generate quality evidence (intermittently or on an ongoing basis) through processes that help us to question positions, unpack assumptions, and make us think more creatively about the role of the law within the broader setting.

Regulators are reasonably well placed to be 'first movers' in this process, but a range of actors are also important 'carriers of agency', and can be rational initiators who not only enable development *through* regulation, but are able to prompt positive regulatory change through participative deliberation *about* regulation (which in turn brings about scientific and social change). Thus, LF relies on a wide range of actors so as to subject the technical field and its trajectories, *together with social trends, and legal conditions, inertias and developments* to early, rational, sober reflection, offering the participants a chance to help *shape the future* by creating pathways into the unknown through regulation.[24] This can be done through a range of mechanisms, including calls for evidence, participative workshops, citizen juries, DELPHI surveys, semistructured interviews, and structured scenario building, and indeed multiple methodologies are recommended. The key is that the effort is sustained and the process is collaborative; expert and lay actors (including non-traditional participants) collectively generate a better and more diverse evidence base in support of more robust and reflexive decision making, thereby better equipping decision makers to *anticipate* movements and *design* moral options for

[22] Alastair T. Iles, *Human Genome Project: A Challenge to the Human Rights Framework*, 9 HARV. HUM. RIGHTS J. 27 (1996), at 57.

[23] This emphasis on legal innovation sets it apart from many other foresighting exercises; it is an exercise concerned with law in society, and with making the law more effective in its social operation and in its relationship with the object of its attention, in this case a dynamic, complex and uncertain science.

[24] Laurie et al., *supra* note 21. See also Brian Wynne, *Uncertainty and Environmental Learning: Reconceiving Science and Policy in the Preventive Paradigm*, 2 GLOB. ENVIRON. CHANGE 111 (1992).

innovation (and the law) that are fit for purpose. So defined, it is clear that foresighting efforts in the legal sphere have been very few.[25]

So conceived, RRI imposes obligations on governments, regulators, and funders to expand dramatically the opportunities for early collaborative engagement around the purposes and directions of science and innovation, and to more explicitly build into research program processes for ongoing reflexivity around actions, obligations, outcomes, trajectories, and also law as a component of governance. In other words, it demands that they pay sustained attention, and offer ongoing and systematic support (read funding), so that actors from across diverse but complimentary fields (ie innovators, healthcarers, patients, IP experts, civil society actors, etc.) can come together on a regular basis to reflect on the field and how it is developing, and how it might develop differently.[26]

VALUE-BASED REGULATION

RRI processes, which could benefit from the LF framework, could and should lead to useful discussions around foundational values. As has been advocated elsewhere,[27] it is important for research undertakings, especially those expected to endure, to identify, and reflect broad values, which serve as signals to stakeholders and publics about what will inform actions and decisions (ie they are both descriptive and normative). While strongly risk-based and autonomy-based approaches have influenced existing structures and practices, a more solidarity-colored approach is warranted in the health research setting. On biobanks, Prainsack and Buyx have argued that:

> A biobank reflective of [solidarity] would pursue assisting others as its main research goal; that is, the main activity of the biobank would always have to be research aiming to improve health of individuals or populations (or comparable, other-directed goals). In addition, transparency towards participants is required about how the goal of improving the health of individuals and populations relates to commercial goals.[28]

Other values are also pertinent to this setting. Some have been espoused in the many international legal instruments that are applicable to biomedicine,[29] including scientific

---

[25] The process of designing the LF framework was an example of partial operation (ie it was an evolving process in practice throughout our work in Argentina). For more on some of this work, see http://www.research.ed.ac.uk/portal/en/projects/governing-emerging-biotechnologies-social-values-and-stem-cellresearch-regulation-in-argentina(77db2184-b88f-47b3-9281-e921ca91ffaf).html.

[26] All of which imposes on researchers an obligation to take much more seriously their deliberative and engagement activities (ie to effectively integrate them into their research activities, and to pursue them genuinely and with a view to real reflexivity).

[27] Harmon, *supra* note 8; Shawn H. E. Harmon, *Solidarity: A (New) Ethic for Global Health Policy*, 14 HEALTH CARE ANAL. 215 (2006); Shawn H. E. Harmon and Aisling McMahon, *Banking (on) the Brain: From Consent to Authorisation and the Transformative Potential of Solidarity*, 22 MED. L. REV. 572 (2014).

[28] Barbara Prainsack and Alena Buyx, *A Solidarity-Based Approach to the Governance of Research Biobanks*, 21 MED. L. REV. 71 (2013), at 77.

[29] Examples include the European Convention on Human Rights (ECHR), the Convention on Human Rights and Biomedicine (Oviedo), the EU Charter of Fundamental Rights (Charter), the Declaration of Helsinki (Helsinki), the ISSCR Guidelines (ISSCRG).

freedom,[30] autonomy,[31] and safety.[32] Others, which were uncovered in the course of a two-year empirical project studying regenerative medicine in Argentina,[33] include the following.

First, with respect to values about society and the role of science generally, 'well-being', 'dignity', 'justice', and 'autonomy' have been cited as critical. Well-being acknowledges that social health and productivity depend on human health; it is important to protect life, health, and wellness, both physical and psychological, and to support actions that facilitate quality of life. Dignity recognizes the importance of respecting people (ie generating knowledge within moral bounds); while pushing boundaries and being creative is important, innovators must balance the research imperative with other values, being careful not to instrumentalize people. Justice refers to the fact that actors must ensure equality and equity, and must share fairly the benefits of research (ie the benefits of research must be made available and optimized). Finally, with respect to autonomy, individuals and communities desire to exercise free will, so creating space for people to make decisions about themselves and for themselves according to their values is important. This demands that stakeholders should be given adequate information so they can weigh options and make reasonably informed decisions, and be satisfied that agents will take reasonable steps to protect their personal information.

Values were also noted as having a particular importance to science and its governance. In this regard, 'integrity', 'transparency', 'engagement', and 'reflexivity' have been highlighted as important. On integrity, researchers must be honest with and about patients and subjects, and with research data. They must not promise to do one thing and then do another, and they must avoid hyperbole and inflated claims. As part of this, they must not put donors, research subjects, or patients at undue risk; researchers should be motivated by non-maleficence (a will to do no harm) and beneficence (an ambition to actively do good), and should avoid unnecessary risks, manage acceptable risks, and improve the quality of life of people. Transparency demands that innovators model comprehensible and open decision-making structures, and encourage information sharing in multiple directions by designing rational structures to manage resources that includes multidirectional communication strategies and periodic reviews of governance practices. Engagement acknowledges that participation and partnership are important. Good science needs more than well-meaning scientists; it requires open, pluralistic debate and idea exchange, and governance structures that encourage this while also providing boundaries. Innovators must therefore pursue ongoing communication with potential donors, participants, and the general public, encouraging participation in the resource, informing about general findings from research based on the resource, and

---

[30] See Article 15, Oviedo; Article 13, Charter; Recommendation 34, ISSCRG.

[31] See Article 10, ECHR; Articles 1, 3 and 24, Charter; Article 5, Oviedo; Articles 22 and 24, Helsinki; Recommendation 28, ISSCRG.

[32] See Article 2, ECHR; Articles 2 and 24, Charter; Articles 5 and 16, Oviedo; Articles 6, 16, 18, 20, 21 and 31, Helsinki; Recommendation 24, ISSCRG.

[33] Shawn H. E. Harmon, *Opinion 4:2010: Guiding Values: Argentine Stem Cell Research and Regenerative Medicine*, Policy Brief for the Argentine Ministry of Science & Technology (2010), http://www2.law.ed.ac.uk/ahrc/esrcvaluesproject/reports.asp; Shawn H. E. Harmon, *Regulation of Stem Cell and Regenerative Science: Stakeholder Opinions, Plurality and Actor Space in the Argentine Social/Science Setting*, 2 L. Innovation & Tech. 95 (2010); Shawn H. E. Harmon, *Ambition and Ambivalence: Encouraging a 'Sci-Tech Culture' in Argentina through Engagement and Regulatory Reform*, 5 Stud. Ethics L. & Tech. 1 (2011).

responding to inquiries about the resource. To be reflexive, governance practices and strategies must evolve if they are to remain optimal. This demands both reflexivity and an iterative approach to both governance and practice mechanisms and processes. Innovators should therefore endeavor to undertake periodic reviews of their governance structures and practices to ensure that they are fit for purpose.

Of course, other values could be added to these, but the point is that they must be collaboratively identified and explored using a robust evidence-generating process (like LF within an RRI setting), and they must then be operationalized.

CONCLUSION

The importance of explicit governance frameworks to our ambitions for the good governance of science (and particularly biobanking) has been emphasized:

> The benefit of governance is that it promotes certainty and efficiency as people know what the rules are, what happens, and when. It can ensure uniformity and equality—that things are done in a uniform way with everyone and the same issues being treated the same. Such a system enables problems to be anticipated as there are mechanisms to deal with the routine issues but unanticipated situations can also be resolved efficiently. Having a governance system in place ensures that ethical and lawful research is supported through accountable and transparent decision making. This not only protects the integrity of the research community but also has the effect of promoting public confidence and trust.[34]

Unfortunately, it has also been found that the majority of existing and emerging biobanks *fail* to adopt a prospective governance strategy.[35] If we hope to achieve good governance for precision medicine—or for any other emerging practice characterized by convergence and uncertainty—then we must acknowledge that governance is enacted by many parties, including those who are themselves governed (ie innovators who are subject to external regulation also construct the governance setting applicable to them through their own standards and actions, their collaborative work with regulators, and the imaginaries and worldviews by which they shape their decisions). This demands new and sustained practices for thinking about governance. The notions of RRI and LF are examples of practices being theorized and put at least partially into operation, but examples of their integration are few, if any. This is lamentable. Perhaps our well-funded pursuits in precision medicine will help achieve the operationalization that we have been missing.

---

[34] Jane Kaye, *From single Biobanks to International Networks: Developing e-Governance*, 130 Hum. Genet. 377 (2011), at 379.

[35] Anne Cambon-Thompson, Emmanuelle Rial-Sebbag & Bartha Maria Knoppers, *Trends in Ethical and Legal Frameworks for the Use of Human Biobanks*, 30 Eur. Respir. J. 373 (2007); Rosario Isasi & Bartha M. Knoppers, *From Banking to International Governance: Fostering Innovation in Stem Cell Research*, 2011 Stem Cell Int'l 498132 (2011).