Afterword

What Could a Learning Health Research Regulation System Look Like?

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1 INTRODUCTION

This final chapter of the *Cambridge Handbook of Health Research Regulation* revisits the question posed in the Introduction to the volume: *What could a Learning Health Research Regulation System look like?* The discussion is set against the background of debates about the nature of an effective learning healthcare system,[1] building on the frequently expressed view that any distinction between systems of healthcare and health research should be collapsed or at the very least minimised as far as possible. The analysis draws on many of the contributions in this volume about how health research regulation can be improved, and makes an argument that a framework can be developed around a Learning Health Research Regulation System (LHRRS). Central to this argument is the view that successful implementation of an LHRRS requires full integration of insights from bioethics, law, social sciences and the humanities to complement and support the effective delivery of health and social value from advances in biomedicine, as well as full engagement with those who regulate, are regulated, and are affected by regulation.

2 LESSONS FROM LEARNING HEALTHCARE SYSTEMS AND REGULATORY SCIENCE

The US Institute of Medicine is widely credited for making seminal contributions to debates about the nature of learning healthcare systems, primarily through a series of expert workshops and reports examining the possible contours of such systems. A central feature of the normative frameworks proposed relies on the collapsing – or at least a blurring – of any distinction between objectives in the delivery of healthcare and the objectives of realising value from human health research. The normative ideal has been articulated as follows:

> . . . a system in which advancing science and clinical research would be natural, seamless, and a real-time byproduct of each individual's care experience; highlighted the need for a clinical data trust that fully, accurately, and seamlessly captures health experience and improves society's knowledge resource; recognized the dynamic nature of clinical evidence; noted that standards

[1] As we go to press, we are heartened to read a blog by Natalie Banner, 'A New Approach to Decisions about Data', in which she advocates for the idea of 'learning governance' and with which we broadly agree. N. Banner, 'A New Approach to Decisions about Data' (*Understanding Patient Data*, 2020), www.understandingpatientdata.org.uk/news/new-approach-decisions-about-data.

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should be tailored to the data sources and circumstances of the individual to whom they are applied; and articulated the need to develop a supporting research infrastructure.[2]

It is the challenge of developing and delivering a 'supporting research infrastructure' that is the core concern of all contributions to this volume. We have stated at the outset that our approach is determinedly normative in tackling what we believe to be the central features of any ecosystem of health research regulation. The structure and content of the sections of this volume reflect our collective belief that the design and delivery of any effective and justifiable system of human health research must place the *human* at the centre of its endeavours. Also, when seeking to design systems from the bottom-up, so to speak, we contend that this human-centred approach to systems must go beyond patient-centredness and exercises in citizen engagement. In no way is this to suggest that these objectives are unimportant; rather, it is to recognise that these endeavours are only part of the picture and that a commitment to delivering a whole system approach must integrate both these and other elements into any system design.

There is, of course, the fundamental question of where does one begin when attempting system design? Each discipline and field of enquiry will have its own answer. As an illustration, we can consider a further workshop held in 2011 under the auspices of the Institute of Medicine and other bodies; this was a Roundtable on value and science-driven healthcare that sought to 'apply systems engineering principles in the design of a learning healthcare system, one that embeds real-time learning for continuous improvement in the quality, safety, and efficiency of care, while generating new knowledge and evidence about what works best'.[3] Once again, these are manifestly essential elements of any well-designed system, but it is striking that this report makes virtually no mention of the ethical issues at stake. To the extent that ethics are mentioned, this is presented as part of the problem of current fragmentation of systems,[4] rather than as any part of a systems solution: '[e]ach discipline has its own statement of its ethics, and this statement is nowhere unified with another. There is no common, shared description of the ethical center of healthcare that applies to everybody, from a physician to a radiology technician to a manager'.[5]

Furthermore, while the Roundtable was styled as being about value- and science-driven healthcare, it is crucial to ask what is meant by 'value' in this context of systems design. Indeed, the Roundtable participants did call for greater enquiry into the terms, but as it was characterised in various presentations and discussions, the term was used variously to refer to:

- *Value* to consumers;
- *Value* from 'substantially expanded use of clinical data';[6]
- *Value* in accounting for costs in outcomes and innovation
- *Value* in 'health returned for dollars invested';[7]
- *Value* as something to be measured for inclusion in decision-making processes.[8]

[2] Institute of Medicine, 'Patients Charting the Course: Citizen Engagement and the Learning Health System' (*Institute of Medicine*, 2011), 240.

[3] National Academy of Engineering, 'Engineering a Learning Healthcare System: A Look at the Future' (*National Academy of Engineering*, 2011).

[4] For an analysis of ethics as a (problematic?) negotiated regulatory tool in the neurosciences, see Pickersgill, Chapter 31, this volume.

[5] National Academy of Engineering, 'Engineering a Learning Healthcare System', 5.

[6] Ibid., 4.

[7] Ibid., 21.

[8] Ibid., 22.

As extensively demonstrated by the chapters in this volume, there is a crucial distinction between 'value' seen in these terms and the 'values' that underpin any structure or system designed to deliver individual and social benefit through improved health and well-being. This distinction is, accordingly, the focus of the next section of this chapter.

Before this, a further important distinction between healthcare systems and health research systems must be highlighted. As an earlier Institute of Medicine report noted, patient-centred care is of paramount importance in identifying and respecting the preferences, needs and values of patients receiving healthcare.[9] This position has rightly been endorsed in subsequent learning systems reports.[10] However, for LHRRS, and from a values perspectives, there is arguably a wider range of interests and values at stake in conducting health research and delivering benefits to society.[11] This is the principal reason why this volume begins with an account of key concepts in play in human health research (see Section IA), because this provides a solid platform on which to conduct multidisciplinary, multisector discussions about what is important, what is at risk, and what accommodations should be made to take into account the range of interests that are engaged in health research. This is a further reason why, in Section IIA, our contributors engage critically and at length with the private and public dimensions of health research regulation.

From this, two important top-level lessons arise from this volume:

- There is considerable value in taking a multi- and inter-disciplinary approach to systems design that places bioethics, social sciences and humanities at the centre of discussions because these disciplinary perspectives are crucial to ensuring that the *human* remains at the focus of human health research; indeed, an aspiration to trans-disciplinary contributions would not be remiss here.
- There is a need for further and fuller enquiry into ways in which the values underpinning healthcare and health research do, and do not, align, and how these can be mobilised to improve regulatory design.

On this last point, we can look to recent initiatives in Europe and the UK that have as their focus 'regulatory science' and we can ask further how the contributions in this volume can add to these debates.

A July 2020 report from the UK advocated for innovation in 'regulatory science' as it relates to healthcare in order to complement the nation's industrial strategy, to enable accelerated routes to market; to increase benefits to public health; to assure greater levels of patient safety; to influence international practice; and to promote investment in the UK (Executive Summary).[12] 'Regulatory science' is defined therein as '[t]he application of the biological, medical and sociological sciences to enhance the development and regulation of medicines and devices in order to meet the appropriate standards of quality, safety and efficacy'.[13] The authors prefer this definition among others as a good starting point for further deliberation and action, both for its breadth and inclusiveness as to what should be considered to be in play. The report offers a very full account of the present regulatory landscape in the UK and offers a strong set of recommendations for

[9] Institute of Medicine, 'Crossing the Quality Chasm: A New Health System for the 21st Century' (*Institute of Medicine*, 2001).

[10] National Academy of Engineering, 'Engineering a Learning Healthcare System', 5.

[11] For an account of ethical considerations in a learning healthcare system, see R. R. Faden et al., 'An Ethics Framework for a Learning Health Care System: A Departure from Traditional Research Ethics and Clinical Ethics' (2013) *Hastings Center Report*, 43(s1), S16–S27.

[12] M. Calvert et al., 'Advancing Regulatory Science and Innovation in Healthcare' (*Birmingham Health Partners*, 2020).

[13] Calvert et al., 'Advancing Regulatory Science,' 6, citing S. Faulkner, 'The Development of Regulatory Science in the UK: A Scoping Study' (*CASMI*, 2018).

improvement in four areas: (i) strategic leadership and coordinated support, (ii) enabling innovation, (iii) implementation and evaluation, and (iv) workforce development. However, a striking omission from the report is any direct and explicit mention of how 'sociological sciences', let alone bioethical inquiry, can contribute to the delivery of these objectives.

Similarly, in March 2020, the European Medicines Agency (EMA) published its strategy, 'Regulatory Science to 2025'. The stated aim is 'to build a more adaptive regulatory system that will encourage innovation in human and veterinary medicine'. For the EMA, regulatory science refers to

> the range of scientific disciplines that are applied to the quality, safety and efficacy assessment of medicinal products and that inform regulatory decision-making throughout the lifecycle of a medicine. It encompasses basic and applied biomedical and social sciences and contributes to the development of regulatory standards and tools.[14]

As with the UK report, however, there is no more than a cursory mention of the concrete ways in which social sciences and bioethics contribute to these objectives.[15]

This returns us to the key questions that frame this Afterword: where is the human in human health research? Also, what would a whole-system approach look like when we begin with the human values at stake and design systems accordingly?

3 FROM VALUE TO VALUES

Currently, there is extensive discussion and funding of data-driven innovation, and undoubtedly, there is considerable value in the raw, aggregate, and Big Data themselves. However, given that in biomedicine the data in question predominantly come from citizens in the guise of their personal data emanating from a growing number of areas of their private lives, it is the contention of this Afterword, and indeed the tenor of this entire volume, that it is ethics and values that must drive the regulation that accompanies the data science, and not a science paradigm. As the conclusion to the Introduction of this volume makes clear, public trust is vital to the success of the biomedical endeavour, and any system of regulation of biomedical research must prove itself to be trustworthy. As further demonstrated by various contributions to this volume,[16] a failure to address underlying public values and concerns in health research and wider uses of citizens' data can result in a net failure to secure social licence and doom the initiatives themselves.[17] This has been re-enforced most recently in February 2020 by an independent report commissioned by Understanding Patient Data and National Health Service (NHS) England that found, among other things, that NHS data sharing should be undertaken by partnerships that are transparent and accountable, and that are governed by a set of shared principles (principles being a main way in which values are captured and translated into starting points for further deliberation and action).[18]

[14] European Medicines Agency, 'EMA Regulatory Science to 2025: Strategic Reflection' (*EMA*, 2020), 5.

[15] For a plea to recognise the value of upstream input from the social sciences and humanities, see M. Pickersgill et al., 'Biomedicine, Self and Society: An Agenda for Collaboration and Engagement' (2019) *Wellcome Open Research*, 4(9), https://doi.org/10.12688/wellcomeopenres.15043.1.

[16] Kerasidou, Chapter 8, Aitken and Cunningham-Burley, Chapter 11, Chuong and O'Doherty, Chapter 12, and Burgess, Chapter 25, this volume.

[17] P. Carter et al., 'The Social Licence for Research: Why *care.data* Ran into Trouble' (2015) *Journal of Medical Ethics*, 40(5), 404–409.

[18] H. Hopkins et al., 'Foundations of Fairness: Views on Uses of NHS Patients' Data and NHS Operational Data' (*Understanding Patient Data*, 2020), www.understandingpatientdata.org.uk/what-do-people-think-about-third-parties-using-nhs-data#download-the-research.

Thus, we posit that any learning system for human health research must be *values-driven*. To reiterate, this explains and justifies the contributions in Section IA of the volume that seek to identify and examine the key values and core concepts that are at stake. Normatively, it would not be helpful or appropriate for this chapter to attempt to suggest or prescribe any particular configuration of values to deliver a justifiable learning system. This depends on myriad social, cultural, economic, institutional and ethical factors within a given country or jurisdiction seeking to implement an effective system for itself. Rather, we suggest that *values engagement* is required amongst all stakeholders implicated in, and affected by, such a system in its given context, and this is the work done by Section IB of the volume in identifying key actors, including publics, and demonstrating through examples how regulatory tools and concepts have been used to date to regulate human health research. Many of these remain valid and appropriate after years of experiences, albeit that the analysis herein also reveals limitations and caveats to existing approaches, for example with consent[19] and proportionality,[20] while also demonstrating the means by which institutions can show trustworthiness[21] and/or conduct meaningful engagement with publics and other stakeholders.[22]

But to understand what it means for a system to be truly effective in self-reflection and learning, we can borrow once again from discussion in the learning healthcare context. As Foley and Fairmichael have pointed out: 'Learning Healthcare Systems can take many forms, but each follows a similar cycle of assembling, analysing and interpreting data, followed by feeding it back into practice and creating a change'.[23] The same is true for a HRRLS. Thus, a learning system is one that consists not only of processes designed to deliver particular outcomes, but also one that has feedback loops[24] and processes of capturing evidence of what has worked *less* well.[25] Self-evidently from the above discussion, 'data' in this context will include data and information about *values failure*[26] or incidents or points in the regulatory processes where sight has been lost of the original values that underpin the entire enterprise.

From the perspective of regulatory theory and practice, this issue relates to the ever-present issue of *sequencing*: when, and at what point in a series of processes should certain actions or instruments be engaged to promote key regulatory objectives?[27] In regulatory theory, sequencing is often concerned with escalation of regulatory intervention, that is, invoking a particular regulatory response when (and only when) other regulatory responses fail. However, this need not be the case. Early and sequential feedback loops in the design and delivery of a system can help to prevent wider systemic failure at a later point in time. This is especially the case if ethical sensitivities to core values remain logically prior to techno-scientific considerations of risk management and are

[19] Kaye and Prictor, Chapter 10 this volume.
[20] Schaefer, Chapter 3 this volume.
[21] Kerasidou, Chapter 8 this volume.
[22] Aitken and Cunningham-Burley, Chapter 11, Chuong and O'Doherty, Chapter 12, and Burgess, Chapter 25 this volume.
[23] T. Foley and F. Fairmichael, 'The Potential of Learning Healthcare Systems' (*The Learning Healthcare Project*, 2015), 4.
[24] Further on feedback loops in the health research context, see S. Taylor-Alexander et al., 'Beyond Regulatory Compression: Confronting the Liminal Spaces of Health Research Regulation' (2016) *Law, Innovation and Technology*, 8(2), 149–176.
[25] For a discussion of a learning system in the context of AI and medical devices, see Ho, Chapter 28, this volume.
[26] For a richer conceptualisation of regulatory failure than mere technological risk and safety concerns, see Flear, Chapter 16, this volume.
[27] See, generally, P. Drahos (ed), *Regulatory Theory: Foundations and Applications* (ANU Press, 2017), and more particularly R. Baldwin et al., *Understanding Regulation: Theory, Strategy, and Practice* (Oxford University Press, 2011), p. 158.

part of risk-benefit analysis.[28] Indeed, as pointed out by Swierstra and Rip, human agency can make a difference at an early stage of development/innovation, when issues and directions are still unclear, but much less so in later stages when 'alignments have sedimented'.[29]

Key among the ethical objectives of any health research system is the need to deliver social value (or at least that prospective research has a reasonable chance of doing so).[30] Some of us have argued elsewhere that there is at present an unmet need to appraise social value iteratively throughout the entire research lifecycle,[31] and this builds on existing arguments to see social value as a dynamic concept. The implications of this for a LHRRS are that the research ecosystem would extend from the research design stage through publication and dissemination of research results, to data storage and sharing of findings and new data for future research. This means that social value is not merely something promissory and illusive that is dangled before a research ethics committee as it pores over a research protocol,[32] but that it is potentially generated and transformed multiple times and by a range of actors throughout the entire process of research: from idea to impact. Seen in this way, social value itself becomes a potential metric of success (or failure) of a learning health research system, and opens the possibility that value might emerge at times and in spaces previously unforeseen. Indeed, Section IIB of this volume is replete with examples of the importance of time within good governance and regulation, whether this be about timely research interventions in the face of emergencies,[33] the appropriateness and timing of effective oversight of clinical innovation,[34] or the challenge of 'evidence' when attempting to regulate traditional and non-conventional medicines.[35]

As a final crucial point about how an ethical 'system' might be constructed with legitimacy and with a view to justice for all, we cannot overlook what Kipnis has called *infrastructural vulnerability*:

> At the structural level, essential political, legal, regulative, institutional, and economic resources may be missing, leaving the subject open to heightened risk. The question for the researcher is, 'Does the political, organizational, economic, and social context of the research setting possess the integrity and resources needed to manage the study?'
>
> ... [c]learly the possibility of infrastructural vulnerability calls for attention to the contexts within which the research will be done.[36]

Questions of the meanings and implication of vulnerability are addressed early in this volume as a crucial framing for the entire volume.[37] It is also clear that this concern is not one for researchers alone. This brings us to the important question of who is implicated in the design and delivery of a LHRSS ecosystem?

[28] On such a systemic exercise for risk-benefit see, Coleman, Chapter 13, this volume. On the blinkered view of regulation that reduces assessments only to techno-scientific assessments of risk-benefit, see Haas and Cloatre, Chapter 30.

[29] T. Swierstra and A. Rip, 'Nano-ethics as NEST-ethics: Patterns of Moral Argumentation About New and Emerging Science and Technology' (2007) *Nanoethics*, 1, 3–20, 8.

[30] See further, van Delden and van der Graaf, Chapter 4, this volume.

[31] A. Ganguli-Mitra et al., 'Reconfiguring Social Value in Health Research Through the Lens of Liminality' (2017) *Bioethics*, 31(2), 87–96.

[32] For a more dynamic account of research ethics review, see Dove, Chapter 18, this volume.

[33] Ganguli Mitra and Hunt, Chapter 32, this volume.

[34] Lipworth et al., Chapter 29, this volume.

[35] Haas and Cloatre, Chapter 30, this volume.

[36] K. Kipnis, 'Vulnerability in Research Subjects: A Bioethical Taxonomy' (2001) *Commissioned Paper*, www.aapcho.org/wp/wp-content/uploads/2012/02/Kipnis-VulnerabilityinResearchSubjects.pdf, 9.

[37] See Rogers, Chapter 1, and Brassington, Chapter 9, this volume.

4 WHO IS IMPLICATED IN THIS ECOSYSTEM, AND WITH WHICH CONSEQUENCES?

In 2019, Wellcome published its Blueprint for Dynamic Oversight of emerging science and technologies.[38] This is aimed determinedly at the UK government, and it is founded on four principles with which few could take exception.

> **Dynamic oversight can be delivered by reforms underpinned by the following principles:**
>
> **Inclusive:** Public groups need to be involved from an early stage to improve the quality of oversight while making it more relevant and trustworthy. The Government should support regulators to involve public groups from an early stage and to maintain engagement as innovation and its oversight is developed.
>
> **Anticipatory:** Identifying risks and opportunities early makes it easier to develop a suitable approach to oversight. Emerging technology often develops quickly and oversight must develop with it. UK regulators must be equipped by government to anticipate and monitor emerging science and technologies to develop and iterate an appropriate, proportionate approach.
>
> **Innovative.** Testing experimental oversight approaches provides government and regulators with evidence of real-world impacts to make oversight better. Achieving this needs good collaboration between regulators, industry, academia and public groups. The UK is beginning to support innovative approaches, but the Government needs to create new incentives for the testing of new oversight approaches.
>
> **Proportionate.** Oversight should foster the potential benefits of emerging science and technologies at the same time as protecting against harms, by being proportionate to predicted risk. The UK should keep up its strong track record in delivering proportionate oversight. These changes will only be delivered effectively if there is clear leadership and accountability for oversight. This requires the Government to be flexible and decisive in responding to regulatory gaps.
>
> Wellcome, A Blueprint for Dynamic Oversight, (2019)

We can contrast this top-down framework with a bottom-up study conducted by the members of the Liminal Spaces team as part of the project funding this volume. The team undertook a Delphi policy[39] study to generate empirical data and a cross-cutting analysis of health research regulation as experienced by stakeholders in the research environment in the United Kingdom. In short, the project found that:

> [t]he evidence supports the normative claim that health research regulation should continue to move away from strict, prescriptive rules-based approaches, and towards flexible principle-based regimes[40] that allow researchers, regulators and publics to coproduce regulatory systems serving core principles.[41]

As a concrete illustration of why this is important, we can consider the last criterion listed as part of the Wellcome Dynamic Oversight framing: proportionality. The Delphi study revealed novel insights about how proportionality as a regulatory tool is seen and operationalised in practice.

[38] J. Clift, 'A Blueprint for Dynamic Oversight: How the UK Can Take a Global Lead in Emerging Science and Technologies' (*Wellcome*, 2019).

[39] On further policy perspectives, see Meslin, Chapter 22, this volume.

[40] On Rules, Principles, and Best Practices, see Sethi, Chapter 17, this volume.

[41] I. Fletcher et al., 'Co-production and Managing Uncertainty in Health Research Regulation: A Delphi Study' (2020) *Health Care Analysis*, 28, 99–120, 99.

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In contrast to the up-front risk management framing offered above, the Delphi findings suggest that proportionality is often treated as an ethical assessment of the values and risks at stake at multiple junctures in the research trajectory. That is, while it can be easy to reduce proportionality to a techno-bureaucratic risk/benefit assessment, this is to miss the point that the search for proportionality is a moral assessment of whether, when, and how to proceed in the face of uncertainty. Furthermore, the realisation that a role for proportionality can arise at multiple junctures in the research ecosystem, including into the phase about data access[42] and potential feedback of results to research participants, highlights that the range of actors involved in these processes are diverse and often unconnected. For example, Delphi participants frequently stated that reporting of adverse events was a downstream disproportionate activity:

> the definitions of adverse events result in vast numbers of daily events being classed as reportable with result that trials gets bogged down in documenting the utter unrelated trivia that are common in patients with some disorders and unrelated to the drug to the neglect of collecting complete and high quality baseline and outcome data on which the reliability of the results depend (25, researcher).[43]

However, this should be contrasted with the possible identity interests of patients and citizens, which can be impacted by (non)access to biomedical information about them, as argued elsewhere in this volume.[44] The ethics of what is in play are by no means clear-cut. The implication, then, is that a regulatory tool such as proportionality might have far wider reach and significance than has been previously thought; as part of a LHHRS this not only has consequences for a wider range of actors, but the ethical dimensions and sensitivities that surround their (in)action must be duly accounted for.

Regarding possible means to navigate growing complexity within a research regulation ecosystem, some further valuable ideas emerged from the Delphi study. For example, one participant supported the notion of 'regulators etc. becoming helpers and guiding processes to make approval more feasible. Whilst having a proportionate outlook' (27, clinician). Other survey respondents called for 'networked governance' whereby, among other things, 'regulatory agencies in health (broadly understood) would need to engage more with academics and charities, and to look to utilise a broader range of expertise in designing and implementing governance strategies and mechanisms' (5, researcher).[45]

Manifestly, all of this suggests that a robustly designed LHRRS is a complex beast. In the final part of this section, we offer regulatory stewardship as a means of better navigating this complexity for researchers, sponsors, funders and publics, and of closing feedback loops for all stakeholders.

Regulatory stewardship[46] has no unitary meaning, but our previous research has demonstrated that examples from the literature nevertheless point to a commonality of views that cast stewardship as being about 'guiding others with prudence and care across one or more endeavours – without which there is risk of impairment or harm – and with a view to collective betterment'.[47] More work needs to be done on whether and when this role is already undertaken within research ecosystems by certain key actors who may not see themselves as performing such

[42] On Access Governance, see Shabani, Thorogood, Murtagh, Chapter 19, this volume.
[43] Fletcher, 'Co-production and Managing Uncertainty', 109.
[44] See Postan, Chapter 23, this volume.
[45] Quotes in Fletcher et al., 'Co-production and Managing Uncertainty', 109.
[46] See G. Laurie et al., 'Charting Regulatory Stewardship in Health Research: Making the Invisible Visible' (2018) *Cambridge Quarterly of Healthcare Ethics*, 27(2), 333–347; E. S. Dove, *Regulatory Stewardship of Health Research: Navigating Participant Protection and Research Promotion* (Cheltenham: Edward Elgar Publishing, 2020).
[47] Laurie et al., 'Charting Regulatory Stewardship', 338.

a task nor receiving credit for it. One of the Liminal Spaces team has argued that ethics review bodies take on this role to a certain extent – empirical evidence from NHS Research Ethics Committees (RECs) in the UK suggests a far more supportive and less combative relationship with researchers than is anecdotally reported.[48] However, by definition, ethics review bodies can only operate largely at the beginning of the research lifecycle – who is there to assess whether social value was ever actually realised, let alone maximised to the range of potential beneficiaries, including the redressing of social injustices relating to health and even health/wealth generation?

Further empirical research has shown that productive regulation is often only 'instantiated' through practice;[49] that is, it is generated as a by-product of genuine cooperation of regulators and a range of other actors, including researchers, attempting to give effect to regulatory rules or statutory diktats. We suggest, therefore, that there might be a role for regulatory stewardship as part of an LHRRS as a means of giving effect to the multiple dimensions that must interact to give such a system of operating in a genuinely responsive, self-reflexive, and institutionally[50] auto-didactic way.

5 WHAT COULD A LEARNING HEALTH RESEARCH REGULATION SYSTEM LOOK LIKE?

In light of the above, we suggest that the following key features are examples of what we might expect to find in an LHRRS system:

- A system that is **values-driven**, wherein the foundational values of the system reflect those of the range of stakeholders involved;
- A demonstrable commitment to **inclusivity and meaningful participation** in regulatory design, assessment and reform, particularly from patients and publics;
- Robust mechanisms for **evidence gathering** for assessment and review of the workings regulatory processes and relevant laws;
- **Systems-level interconnectivity** to learn lessons across regulatory siloes, perhaps supported by a robust system of **regulatory stewardship**;
- **Clear lines of responsibility and accountability** of actors across the entire trajectory of the research enterprise;
- Coordinated efforts to ensure **ethical and regulatory reflexivity**, that is, processes of self-reference of examination and action, requiring institutions and actors to look back at their own regulatory practices, successes and failures;
- Existence of, and where appropriate closing of, **regulatory feedback loops** to deliver authentic learning back to the system and to its users;
- **Appropriate incentives** for actors to contribute to the whole-system approach, whether this be through recognition or reward or by other means, and eschewing a compliance culture that drives a fear of sanction supplanting it with a system that seeks out and celebrates best practice, while not eschewing errors and lessons from failure.[51]

[48] Dove, 'Regulatory Stewardship'.

[49] N. Stephens et al., 'Documenting the Doable and Doing the Documented: Bridging Strategies at the UK Stem Cell Bank' (2011) *Social Studies of Science*, 41(6), 791–813.

[50] On institutional perspectives on regulation, see McMahon, Chapter 21, this volume.

[51] Evidence of the need for such incentives is presented in A. Sorbie et al., 'Examining the Power of the Social Imaginary through Competing Narratives of Data Ownership in Health Research' (2021), Journal of Law and the BioSciences, https://doi.org/10.1093/jlb/lsaa068.

- **Transparency and demonstrated trustworthiness** in the integrity of the regulatory system as a whole;
- **Regulatory responsiveness** to unanticipated events (particularly those that are high risk both as to probability and as to magnitude of impact). The COVID-19 pandemic is one such example – the clamour for a vaccines puts existing systems of regulation and protection under considerable strain, not least for the truncated timeframe for results that is now expected. Values failure in the system itself is something to be avoided at all cost when such events beset our regulatory systems.

6 CONCLUSION

As indicated at the outset of this volume, the golden thread that runs through the contributions is the challenge of examining the possible contours of a Learning Health Research Regulation System. This, admittedly ambitious, task cannot be done justice in a single Afterword, and all chapters in this volume must be read alone for their individual merit. Notwithstanding, an attempt has been made here to draw elements together that re-enforce – and at times challenge – other work in the field that is concerned with how systems learn and to suggest possible ways forward for human health research. And, even if the ambition of a fully-integrated learning system is too vaulting, we suggest nonetheless that adopting a Whole System Approach to health research regulation can promote more joined-up, reflective and responsive systems of regulation. By Whole System Approach we mean that regulatory attention should be paid to capturing and sharing evidence across the entire breadth and complexity of health research, not just of what works well and what does not, but principally of identifying where, when, and how human values are engaged across the entire research lifespan. This approach, we contend, holds the strongest prospect of delivering on the twin ambitions of protecting research participants as robustly as possible while promoting the social value from human health research as widely we possible.