What does it mean to take an ethics+ approach to global biobank governance?

What Does It Mean to Take an Ethics+ Approach to Global Biobank Governance?

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Abstract: This article re-examines and fundamentally re-assesses the symbiotic relationship between law and ethics in the governance and regulation of biobanks as a global phenomenon. Set against the two decades of experience of set-up, management, and most recently granting access to biobanks to promote advances in human health, it is argued that the boundaries – and so the legitimacy – of the respective roles of ethics and law have become blurred and, potentially, blunted. The caricature of law as a tool of command and control – resulting in compliance culture – is well-recognised in regulation studies, but parallels with this can now also be seen within certain ethical regimes pertaining to biobanks, and human health research more generally. At the same time, the ethical content of certain legal responses to biobanks can be lacking, as some legal systems seek to regulate biobanking in inflexible and unreflective ways that potentially undermine the entire enterprise. This can result in a net failure to capture adequately particular features of biobanking that make this field so potentially rich in terms of ultimate social value and human benefit. The argument is made that the interconnected, yet distinct, nature of the contributions of law and ethics must be better understood in this setting. The central message is unapologetically sceptical about the role of law in regulating biobanking, except when we see law as *process*. Rather, the position is advanced that more work is required to develop governance regimes that are "Ethics+", that is, rooted in the core values and principles at stake while able to adapt and accommodate the inevitable changing landscape of biobank research and practice. While ethics are always a necessary component of a robust and defensible regimes of health research, the notion of Ethics+ directs our attention to processes in which ethical discourse and engagement can be optimised to respond to particular features of biobanks and their operation.

Keywords: biobanks; ethics; law; governance; regulation; process; processual; liminality

Introduction

This article focusses its attention at the crossroads between overlapping, yet conceptually distinguishable, concepts such as law and ethics, and regulation and governance. By 'law' the article adopts a positivist notion of rules made by democratic processes and institutions; by 'ethics' the article appeals to the values, principles and approaches that support critical reflection on the good life and that can be action-guiding. Normatively, the position is taken that law ought to be ethically defensible. Equally, law and ethics, in these terms, are not merely interchangeable. Law might be criticised for its lack of ethical substance, and ethics might guide action in the absence of law (or in ways different to what law prescribes). The article is concerned with what can be called a symbiotic relationship between these two concepts, and it seeks to examine how that relationship might be better understood in one particular context, namely, the operation of biobanks containing human material and data. Furthermore, in order to tease out the nuances of this relationship, the article also seeks to explore the symbiotic relationship between regulation and governance, once again in the biobank context. As with discussions of ethics and law, appeals to regulation and governance are often used interchangeably, but in this article their particular contributions are explored to examine the nature of each, as well as any overlaps between them (both legitimate and illegitimate). For these purposes, the term 'regulation' refers to approaches to biobank management that are either dictated by law or are more law-like, for example, that take the form of top-down, state-driven, prescribed rules or practices, requiring conformity. Normally, in such models sanctions also apply for non-conformity, such as the force of the criminal law. In contrast, 'governance' is used here to refer to a wider set of processes that are both about steering behaviour, and also about broader social concerns such as transparency, accountability and – importantly – ethical credibility (Braithwaite et al, 2007). Governance models may or may not engage the law, but they do have resonance with ethics, as articulated above. This is because they are concerned primarily with delivery of 'good governance' as a supererogatory objective that often exceeds the mere prescription of law. Thus, from this brief account we can see that the concepts of law and ethics, and regulation and governance, overlap and

intertwine, but we do not yet fully understand that nature and consequences of these interactions. This is the problem that is engaged by this article.

No claim is made here that these approximate definitions are accurate in all cases, nor that we cannot find examples that defy this rubric. Rather, this heuristic is offered as a means of engaging with current practices in the oversight and management of biobanks in an attempt to understand and disentangle the nature of the range of approaches that we find in the field.

The argument is made that there is a missing component in our understandings of these approaches. This element is an appreciation of process, or more accurately the *processual*. Thus, while 'process' can be taken to refer to '[a] series of actions or steps taken in order to achieve a particular end' (OED, 2017), attention to the processual is much more about the dynamics and the (inter)actions of the actors engaged in processes. For example, what does it mean for regulators to seek conformity with regulatory processes? Conversely, what does it mean for researchers to be subjected to regulatory processes? The concern, then, is with the experiential elements of regulation and governance; that is, of giving effect to law and/or seeking to act ethically. To capture this, the term 'processual governance' is used. Governance is preferred to regulation in the current context because, as will be seen below, many biobanks are not regulated in the strict law-like manner described above. If we see governance as a wider notion that regulation, that a focus on processual governance also captures instances where law and regulation also have a role. The importance of seeking to understand governance in processual terms is that processes and actors change over time – and this is particularly true for biobanks. A failure to appreciate the implications of this is likely to raise future problems for the effective management of biobanks. Moreover, as will be argued below, this approach further assists in our understanding of the symbiotic relationships between law and ethics, regulation and governance by better identifying the respective spheres of influence, and where undue burden might be reduced, and added value might be introduced.

The article proceeds as follows: (i) an account is given of the phenomenon of biobanking as it has developed in the course of the last two decades. Particular attention is paid to the example of UK Biobank both as one of the longest standing biobanks, and also because of particular features of its governance model; (ii) the example of UK Biobank is then contrasted with other novel governance models, and the question is asked how far, if at all, do the examples under scrutiny embody processual governance; (iii) the lens of processual governance is thereafter used to contrast a governance-based example such as UK Biobank with a more rule-based regulatory example as shown by the experience in Taiwan; (iv) the example is then offered of appeals to social value in ethical discourse to suggest that this discourse is taking an increasingly law-like turn and becoming more regulatory in its outlook; this conceptual and practical confusion is lamented to the extent that it might represent undue regulatory burden in a biobanking context, (iv) finally, and in contrast to the last point, the argument is made that a concept of Ethics+ is to be preferred. This reorients our attention towards the particular value that governance can add to biobank management while also ensuring that appeals to ethics are complementary to any role for law, rather than merely a duplication thereof.

Biobanks as a global phenomenon and a challenge to processual governance

Biobanks are collections of tissues and other samples, often linked to citizens' data, and held as resources to promote health-related research (see generally: Kaye et al. 2012). UK Biobank[1] is one of the best-known and better managed research resources of its kind anywhere in the world. It began life as the Population Biomedical Collection in the latter part of the last century (for a discussion and comparison with the Icelandic database at the time, see: Kaye and Martin 2000), at a time when the prospect of a large-scale, long-term,

[1] http://www.ukbiobank.ac.uk/

longitudinal initiatives of this kind were thought to raise a host of novel ethical and legal challenges. This was not because longitudinal projects exploring genetic origins of disease had not already been established – and some very successfully so (e.g. ALSPAC[2]) – but because UK Biobank was unique in a number of respects. First, the funders were clear that it was not a 'study', that is, it was not focussed on any particular diseases or set of conditions, and, secondly, it was determinedly open-ended in its objective of creating a research resource that would ultimately attract high-quality scientific applications from around the world. Thus, openness and uncertainty were central to UK Biobank from its inception. The uncertainty extended across all aspects of the project from the nature of the proposition being put to participants (what would it mean in the long-term to participate in UK Biobank?), to questions about the management of the resource itself (what unforeseen obligations might arise to participants, and others, once the resource was established?), to matters of genuine global reach (who might seek access to this research resource, for what purposes, at what time, and to what ends?). However, this fluidity also presented an opportunity to develop appropriate oversight and protection safeguards in tandem with the scientific protocol itself. Indeed, it demanded an in-parallel approach. In order to deliver this, the funders established an Interim Advisory Group (IAG), chaired by Dr William Lowrance, and of which I was privileged to be a member together with a previous editor of this journal, Professor Alastair V. Campbell, among others. A key outcome of that process,[3] was the production of a draft Ethics and Governance Framework (EGF) that was then subjected to public consultation (for a brief outline as part of the consultation process for the first draft of the EGF, see: UK Biobank 2004). It formed the basis of the EGF that was eventually adopted by the funders in 2006 and which remains the constitutional document of UK Biobank today. All of this happened against a backdrop of extensive legal reform that culminated in the human Tissue Act 2004, discussed below. However, the position was taken – by the funders and the IAG alike - that while UK Biobank would of course be required to comply with any enacted law, no specific law was required to govern UK Biobank itself. Moreover, the EGF was seen as adding value on top of any legal regime, irrespective of its form or content. The role of the EGF is to articulate the nature and the range of obligations that UK Biobank owes, first and foremost, to its 500,000+ participants,[4] and more widely to society that will ultimately benefit from research conducted using the UK Biobank resource.

A further key recommendation of the IAG was the establishment of an Ethics and Governance Council (EGC) to oversee compliance of the EGF by UK Biobank. This body was established as, and remains, a critical friend to UK Biobank: independent in its operation and with no direct power to require compliance with the EGF. Rather, the model is one of iterative interaction, dialogue, and engagement between members of the EGC and the senior management of UK Biobank to reflect on the on-going fitness-for-purpose of the EGF to capture UK Biobank's responsibilities to participants and to the wider society in the pursuit of the overarching objective to create a viable research resource in the public interest. Perhaps most importantly, the governance arrangements of UK Biobank and its relationship with its Ethics and Governance Council, allow real time interactions and ethical reflection about how UK Biobank should respond to novel issues in the management of the resource that were never previously anticipated. For such reasons, they will not be contained in the original text of the EGF itself (or subsequent versions thereof). In this sense, the EGF is a true 'living instrument', conceived to be subject to on-going revision as necessary over time. I have referred elsewhere to this process as reflexive governance: '... [it] is both about partnership in governance in the face of future uncertainty and the facilitation of mutual learning for experience over time.' (Laurie 2011).

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[2] Avon Longitudinal Study of Parents and Children (ALSPAC): http://www.bristol.ac.uk/alspac/

[3] The process is described on http://www.ukbiobank.ac.uk/ethics/ thus: "The first public draft of the Ethics and Governance Framework (EGF) was developed with the advice of an Interim Advisory Group which met three times between February and July 2003. The group included experts in research ethics, philosophy, law, science and social science, and consumer representation, and was chaired by Dr William Lowrance, a consultant in health policy and ethics."

[4] Recruitment took place between 2007 and 2010. This coincided with the period when I acted as Chair of the EGC, taking over from Alastair Campbell who was the first incumbent in the role from 2004 to 2006.

This article offers an analysis and a defence of such a model. Put otherwise, it represents a call to adopt a *processual* approach to regulation and governance (Taylor-Alexander et al. 2016). As articulate above, such an approach focusses on the experiences of governing, both for those in such a role and for those subject to governance. As such, it is much more than simply identifying elements of process or, indeed, of seeking to map out elements of process in some kind of linear fashion. First and foremost, a processual approach requires a clear and common understanding of the objective, that is, the outcome or *telos* of the process itself: what is the endpoint that we seek to reach? What are the governors and the governed seeking to achieve in common, and what action is required of them to do so? For a project like UK Biobank there are multiple endpoints: it is the establishment of a high-quality research resource; it is the ultimate realisation of improvements in human health arising from use of that resource; and it is the delivery of good governance itself at every stage of these processes, including during times of uncertainty or at strategic crossroads. It is a given that protection of participants is a central consideration in all of this, but like so many other human health research initiatives, it is equally about the promotion of research itself. And perhaps most importantly, a processual approach involves acknowledgement that research processes necessarily change over time – by their very nature they are uncertain and open-ended – and because of this we must be prepared, and able, to respond to novel situations in light of experience (Laurie 2017). Thus, while actors and processes might change and evolve – for example as a result of engagement on novel challenges or with the resolution of a particular conflict – processual governance must be able to capture and learn from all of the experiences involved. A dynamic such as that between UK Biobank and its Ethics and Governance Council allows this to happen. Where once, in the early stages, a strict no feedback policy was in place, this has been revisited and revised after extensive discussions between both parties, and also with the advent of imaging on large sections of cohort. This was not merely an example of a change of policy or process; it was the outcome of discussion and engagement, and of dialogue and occasional disagreement. During my time as EGC Chair, we engaged with radiologists and radiographers on their experiences of capture images, and this fed into the processual governance dynamic. While the membership of the EGC from that time has now almost completely changed, the learning from the processual engagement now forms part of UK Biobank's overall governance approach. Most importantly, it has changed the nature of the relationship between UKB and its participants, resulting in a feedback policy that now conforms more closely with contemporary ethical thinking.

How far do we currently recognise processual approaches to regulation and governance?

Within the existing literature, there is now a plethora of examples of biobanking initiatives that captures some features of this processual approach to regulation and governance. For example, in the context of the UK10k initiative, Kaye et al. (2015) have written about 'pop-up' governance for this large interdisciplinary genomics research consortium exploring rare conditions and which has the primary objective of establishing an accessible resource of sequence data. The key processual element in this example was the temporally limited nature of governance mechanisms that were designed, appeared, and disappeared based on project's need at a given time. While the broad architecture of the project was in place, the need for additional governance input was experience-led; no permanent or standing (and potentially costly) 'oversight body' akin to the UK Biobank's EGC was necessary. The arrangements occurred by mutual consensus between trusted parties for as long as required.

In the heterogeneous US environment, Cadigan et al. (2017) conducted a study of 456 US biobanks seeking evidence of 'forward-thinking'. In particular, they asked: "Do biobanks enact policies and plans that allow them to anticipate and respond to potential challenges?" In exploring whether either of two policies were in place (return of results and designating ownership of specimens/technology) and/or whether either of two plans were in place (formal business plan and formal closure plan), they found that a tendency for the existence of plans together, and the same was true for the co-existence of plans. However, only 7% of biobanks had all four governance features in place, and 12% had none. The authors conjecture that the (co)existence of the policies suggests responsiveness, while the (co)existence of plans suggests attention to sustainability.

In the regional European context, various initiatives exist (see for example: Kaye et al. 2016a), and notable among these is the Biobanking and BioMolecular Resources Research Infrastructure-European Research Infrastructure Consortium (BBMRI-ERIC) (Mayrhofer et al. 2016). Among its many governance innovations, from a processual perspective, there is the common objective of delivering 'technical alignment' of European biobanks in terms of sharing and interoperability; that is, that data and samples are held, accessed, and used in ways that a scientifically compatible and meaningful. The technical processes involved – through the MIABIS[5] model – cover the full gamut of biobank operations from categories of information and samples, to data infrastructures, to articulation, agreement and adoption of common standards on issues as diverse as data quality, security, privacy and consent processes for recruitment. But, as Tamminem (2015) has argued, the biological, the philosophical and the political are intertwined:

> Thus, the network formed through digital tools, the new biobank lexicon, and architectural labours redefines the 'bio-objects' held by biobanks in and through the MIABIS model. It is not unifying or totalising in nature. It is instead aggregative and intensifies biological knowledge. This network ties biobanks together in a way that enables new types of bio-objects and bio-objectification practices to emerge by means of the virtual database. In the BBMRI, biological bodies become informational objects composed of digital technologies aimed at fulfilling the promise of European research policy, essentially based on a vision of a distributed infrastructure … The vision transcends national legislation, policy, and local languages, and it creates a supranational virtual population, whose seat of life is not in the organism but in the database, resisting reduction to existing local, biological, and legal forms of life.

Processes of digitisation beget, in turn, processes requiring novel transnational governance that is responsive to what the 'supranational virtual population' might *become*.

To support and accommodate such moments of *becoming*, the work of the Global Alliance for Genomics & Health (GA4GH) is also important. It has been invaluable in providing its stakeholders around the world – be they researchers, regulators, national states or other parties – with an armamentarium of tools (Global Alliance for Genomics and Health n.d.) designed to promote closer and better technical and governance interoperability focussed particularly on responsible data sharing at a global level, while taking a human rights approach. The Alliance's interest in process here is in the process of becoming ready to share data well, widely, and responsibly while operating with local and international legal regimes.

I have stressed the notion of 'becoming' rather strongly in the last few paragraphs. I have done so because I argue that it is crucial to a full account of effective processual governance and regulation. An emphasis on becoming also reminds us of the importance of capturing the experiential – and this is at the hear tof the processual governance approach advocated in this article. The specific examples offered here are merely illustrative, but they are linked by the common objective of realising the operational telos of biobanks: to become a viable and valuable research resource. From a conceptual and operational standpoint, the challenge is to steward 'raw' materials, such as human samples and medical data, towards a new entity – a new ontology – 'the biobank'.

What does it mean for law and ethics to take a processual approach to governance?

Underlying all of these models and the extensive literature that has been written in this field in the last two decades, is the self-evident importance of respecting relevant laws and behaving ethically at all stages of the processes in question. But such is the axiomatic obviousness of these requirements, that we find little

[5] Minimum Information About Biobank Information Sharing (MIABIS): http://www.bbmri-eric.eu/news-events/miabis-2-0-published/

discussion in the literature about what it means for law and ethics to design and implement these biobank governance processes (compare: Ashcroft 2003). Most particularly, we must ask whether, and how, law and ethics assist in these processes, and if they do not, then what ought to be done to address this?

Let us begin with Law and a return to the example of UK Biobank. It is important to observe that UK Biobank was established, and continues to operate, without any specific legislative intervention. That is, there is no UK Biobank Law, nor indeed is there any biobank law in the UK. Rather, UK Biobank – like all other health-related research initiatives operating within the United Kingdom – is subject to a plethora of laws ranging from data protection to human tissue to clinical trials regimes, and across many aspects of the common law, including confidentiality, consent and negligence; we can add further to this list the fields of charity and corporate laws governing the functioning of the legal entity itself. Neither the UKB funders, nor the UK Biobank IAG, nor any government agency thought it necessary to institute a biobank-specific law, and the enterprise has survived – thus far – major legal changes in the guise of wholesale reforms brought about by the Human Tissue Act 2004 and the General Data Protection Regulation, due to be implemented in May 2018.

The same has not been true in other legal systems, and it is easy to find a range of examples of legislative attempts to regulate biobanks (for a European comparative analysis, see for example: Kaye et al. 2016b). In keeping with the focus of this journal, however, let us briefly consider one Asian example. In Taiwan, the first biobank to be established by Academica Sinica was Taiwan Biobank, initiated in 2005 and formally established in 2012 after a series of assessment projects. Initially, it closely followed the UK Biobank model in terms of its governance arrangements: there was an Ethics and Governance Framework and an associated Ethics and Governance Council. Over time, and as reported in 2015, some 25 biobanks have been set up with the approval of the Ministry of Health and Welfare (Fan et al. 2015). The Human Biobank Management Act (Biobank Act) was enacted on 7 January 2010 to sit on top of existing laws and regulations already applying to any biobank enterprise. The 2010 Act was followed by more cumulative legal provision in the guise of the Human Subject Research Act 2011 (Subject Research Act). All must be read together and in addition to more fundamental laws, such as the Indigenous Peoples Basic Law and the Personal Information Protection Act. The navigation of the multiplicity of such laws should not be daunting to the well-trained lawyer, but for the purposes of the objectives of this article, such a legislative morass must be subject to particular scrutiny in processual terms. Take, for example, two illustrations. First, the Biobank Act foresees the operation of broad consent to accommodate the uncertainty of as-yet unknown future uses of the biobank resource; yet, the Subject Research Act mandates consent as a process driven by adequacy of information at the time of recruitment to a particular research project (informed consent); put otherwise, the legal systems construct different consents differently (see further: Fan and Lin 2013). Second, while the Biobank Act sets up an Ethics Committee with a similar 'critical friend' role to the UK Biobank Ethics and Governance Committee, the Subject Research Act mandates institutional review board (IRB) approval for all human subject research. While not necessarily in conflict, these diverse functions have received comment thus (Fan et al. 2015, p. 821):

> With regard to access to materials or data from the biobank, research projects that intend to use resources should be submitted for prior ethics review by the IRB. After review by the IRB, the EGC will review and decide whether the research project should be permitted to access resources from the biobank.

Fundamentally, we must ask here: what do the processes of obtaining consent and undertaking ethics review seek to achieve? In the Taiwan example, are these processes of consent and ethics review simply divergent means towards the same ends, or are they different processes with their own objectives, confusingly with common names? On one view, the answers to these questions do not matter because the rules of these laws are made to be obeyed. Crudely, a positivistic approach to regulation through a command and control model set down in law will require compliance. Moreover, there is no suggestion of hierarchy between such laws, and in this sense the Taiwan and the UK experiences can be contrasted. Taiwan has reduced governance to rules and compliance; the UK has base legal rules that must be followed by virtue of pre-existing wider legal frameworks such as the Human Tissue Act 2004, while the governance regime of UK Biobank sits within, but also apart from, those rules. If there is conflict, the rules will win out. Moreover, the divergent bases for the rules (hard law) and the oversight processes (soft governance) allow for – and might promote – more

reflection on the ways in which these different mechanisms might be designed to achieve different, and complementary ends.

There has been much discussion over the years on the nature of, and need for, broad consent in biobanking and associated ethical oversight. But the ethical basis of these governance tools was already well-established in the early days of biobanking and captured by Alastair V. Campbell (2007, p. 233) when he wrote of the biobank recruitment process, thus:

> … the way in which people make decisions in these circumstances relates much more to their overall values, and their trust in those seeking consent, than to any philosophical account of adequate information forming the basis of valid consent. People can choose to trust, and, provided the structures are in place to ensure that that trust is not betrayed, it is not clear why they should not be free simply to make that choice.

Here, Campbell identifies three crucially important processes: (i) supporting research participants to give meaningful expression to their values, (ii) delivering consent mechanisms – such as broad consent – that reflect those values and do not attempt to reduce consent to mere information disclosure, and (iii) the necessary parallel processes of robust ethical oversight and governance that is focussed on the participants themselves, and the trust that they have given, and not on the compliance with some rule of law.

I argue that attempts to reduce such dynamic and deliberative processes to law are ultimately flawed. Writing back in 1978 on law as process, Sally Falk Moore (1978[6], p. 4) put it thus:

> If partial rule by rules is all that can ever be managed, the fact has considerable import for planning and regulation. Awareness of the limitations on regulation should affect the research objective of those responsible for drawing up rules, predicting their effects, and monitoring their application. A central concern of any rule-maker should be the identification of the social processes which operate outside the rules, or which cause people to use rules, or abandon them, bend them, reinterpret them, side-step them, or replace them. To recognize that such processes are inescapable aspects of the use of rule-systems and to try to understand as much as possible about the conditions of their operation would probably be far more effective than taking the view that such activities might be fully controlled simply by tighter drafting of 'loophole-less' legislation. Social transactions usually take place in the service of objectives to which legal rules are merely ancillary shapers, enablers, or impediments. Conformity to the rules is seldom in itself the central objective.

At one level, it is important to recognise that this means that sometimes Law as legislation is required as a product of social and cultural contexts, and this might well be true for the example of Taiwan above. On another level, however, it is a call to look beyond law – however it is manifested – and to seek to understand the wider social processes and the need for interaction and dynamics in the development of such processes. In the biobank context, these social processes are essentially ethical processes about fundamental respect for persons as participants in human health research; for the trust that they show to biobank managers and data controllers as custodians of their samples and data; and about the ethical process of bringing about social value from these initiatives and from the act of participation itself. Processual governance, with its focus on the experiences of giving effect to these objectives, embraces the fact that there might not always be an immediately obvious 'process' by which to deliver on these elements; it accepts that there might be legitimate disagreement about which policies or processes ought to be adopted, and it reflects the fact that governance is a dynamic interaction in itself, and not a static, formalistic or formal compliance-based framework for delivering the benefits of biobanks. Over time, processual governance also allows for – and can capture – changes of thinking, changes of personnel, and changes of circumstances. This is not to suggest

[6] I am grateful to my colleague, Edward S. Dove, for drawing this title to my attention.

that law does not also do so, but it is well understood that law reform moves at a glacial pace. Processual governance can be more responsive to the time element in biobank management and operation.

Social value in human health research: a means or an end?

A good example of the importance of the time element in this discussion, and of how responsive governance can add value is by revisiting the fundamental notion of social value. A recent special issue of Bioethics (Rid and Shah 2017) has examined the concept and phenomenon of social value in health research, and in that issue I argued with other colleagues (Ganguli-Mitra et al. 2017) that we ought to see social value itself as a transformational process that changes over time. The promissory nature of a research protocol before an ethics committee or institutional review board will not necessarily - if ever – accurately reflect the eventual social value that comes from research, once completed. Moreover, in ethics and governance terms, an up-front requirement in health research regulation that there be social value is relatively meaningless unless the scientific, ethical and social processes can be followed over time with the development of the research itself. As we argue (Ganguli-Mitra et al. 2017, p. 90):

> The multiple, processual changes in research create new avenues for value, new entities that are valuable, new actors to generate or steward value, new populations to whom value may accrue, and new pathways for generating further social value...The lessons learned from Ebola have directly influenced the ways in which the WHO [World Health Organization] is considering R&D for the more recent Zika virus outbreak, establishing frameworks and coordinating activities with the industry and groups studying medicinal responses to Zika.

Notwithstanding, a key message that I want the reader of this paper to take away is this: neither law nor ethics tends to adopt the processual approach I advocate in this contribution. Indeed, the tendency in ethical instruments in recent years – following an explosion of legal regulation in the field of health research – has been to take a far more prescriptive, law-like turn in their outlook. I am concerned that this can misguide us as to what is truly at stake, and divert our attention from the processes involved. In doing so, we run the risk of adding to rules and rule-like frameworks in cumulative ways that will never be able to reflect the social transactions spoken of by Falk Moore, above.

The legalistic turn in bioethics and best practice

A range of examples exists that demonstrate this legalistic turn in bioethics and best practice. This is true across the broad field of bioethics, and particularly so in the context of human health research. Consider the ways in which guidance from professional bodies, such as the UK's General Medical Council (n.d.), the American Medical Association (n.d.), the Australian Medical Association (n.d.), and the Singapore Medical Council (n.d.), have expanded considerably in recent years. The British GMC, for example, has long been vexed by its own use of the language of 'should' and 'must' in its guidance. For the professional, this turns an instrument of support for clinical judgment into yet another prescriptive code of compliance. Internationally, we have seen the unrelenting widening and deepening of content in texts such as the Helsinki Declaration (World Medical Association 2013) and the CIOMS Guidelines, the last most recently revised in 2016 (Council for International Organizations of Medical Sciences 2016). We will return to this example presently. Finally, in the biobank context, we have witnessed the emergence of new guidance from bodies previously unconcerned with health-related research, and the example from the Organisation for Economic Cooperation and Development (OECD) (2009) is apt in this regard.

Taken alone, none of these initiatives is to be lamented; nor is the specific content of each instrument likely to be contentious in its own terms. The concern is the clogging up of the regulatory landscape, making it increasingly difficult for researchers to navigate without fear of sanction from one quarter or another. Most worrying, however, is the rule-like nature with which such instruments are drafted – or indeed interpreted in action. Mere guidance can soon take on the mantle of obligation. Advice to capture instances of best practice can soon become non-negotiable additional measures of compliance. The net effect of this, in my

opinion, is a legalistic turn in bioethics and best practice. What is lost as a result is practical and effective support in navigating increasingly-complex regulatory landscapes.

As an example, let us return to the concept of social value are articulated in the current iteration of the CIOMS Guidelines (Council for International Organizations of Medical Sciences 2016). Consider paragraph 2 of Guideline 1 (scientific and social value and respect for rights):

> Although scientific and social value are the fundamental justification for undertaking research, researchers, sponsors, research ethics committees and health authorities *have a moral obligation to ensure that all research is carried out in ways that uphold human rights, and respect, protect, and are fair to study participants and the communities in which the research is conducted*. Scientific and social value cannot legitimate subjecting study participants or host communities to mistreatment, or injustice. [emphasis added]

Moreover, the Preamble states: 'As a general rule, "must" has been used to attach greater moral weight to requirements when compared to "should".'

This framing, despite the appeal to moral obligation, is increasingly rule-like; I wager it will increasingly be read as such. Of course, this is not to suggest that respect for fellow human beings and their rights should not be forthcoming, but this prescription is well grounded elsewhere in multiple legal instruments.

Regulation or governance?

My diagnosis in all of this is that we fail, increasingly, to differentiate between regulation and governance as outlined at the beginning of this article; and that we fail to recognise the respective contributions of law and bioethics to those respective processes. While I do not wish to suggest that there are fixed and immutable definitions of either 'regulation' or 'governance', there are characteristics that help us differentiate between the two as approaches in themselves as to how we can best deliver responsible health research regulation. Thus, regulatory models will tend to have a basis in law, will tend to include a role for state actors (or sponsorship by the same), will tend to carry a hard sanction function, and will tend towards mechanisms of compliance. Crudely, then, we can expect to find features that are more top-down with respect to any health research initiative. Governance, on the other hand, is more typified by bottom-up approaches. The tend to be less reliant on a legal authority or legal agents, more likely to engage stakeholders on their own terms and experiences, and be more amendable to co-production of effective pathways through a landscape and towards effective health research outcomes. This is what I mean by the Ethics+ approach in the title of this article.

What does it mean to take an Ethics+ approach?

It should be obvious by now that inherent to the central argument of this piece is *process*. A processual approach puts all of this analysis in context. Here, *process* must be distinguished from *procedural*. Procedural compliance can quickly become very law-like. This is not my concern. My use of the term "Ethics+" is an attempt to move beyond such thinking, and the kinds of behaviours that this thinking can engender. Procedural compliance can suggest that all of the ethics work and thinking and judgment has been done simply by following the procedures that are laid down. A processual approach does not offer such an apparently easy ethical get-out.

Ethics+ – as a processual phenomenon – requires reflection and deliberation on each step of a process; it requires the identification of a telos for the process in question, and mechanisms for recalibration if novel events arise that might divert the actors from their course. Ethics+ reflects features of governance that are identified above – for example, engagement with stakeholders on their own terms and experiences, and co-production of pathways through the research process itself. Once again, the example of social value is pertinent. The process towards the realisation of social value will not be clear from the start of the research endeavour. It will change course as the research progresses. Different gatekeepers will offer input at different

junctures – the research ethics committee or IRB will likely help to craft the prospect of social value at the start of the research process, but very different actors must be involved later in the process to give effect to the actual value that the research produces.

This has been recognised to an extent in the bioethics literature, among others by Emanuel and colleagues (2008, p. 127):

> Priorities may change while a study is being conducted, and the cooperation of diverse groups is often needed to make changes based on research results. This makes the process of going from research to health improvements uncertain and arduous. Assessment of the value of research is made prospectively before any data are collected. Consequently, determinations of social value are uncertain and probabilistic, entailing judgments about the usefulness of a sequence of research and chances of implementing the results. Even in wealthy countries with well-established research studies and health system infrastructures, research results are imperfectly incorporated into clinical practice.

The added value of the current analysis, however, is to bring this recognition together within the surrounding ethical, legal, human rights and stakeholder landscapes. In some senses, an Ethics+ approach embraces the uncertain and 'liminal' nature of the health research journey (see further: Laurie 2017). It admits value-based objectives that can act as foci for law, ethics, and stakeholders alike. For example, Dove and Özdemir (2015) have argued that a focus on trustworthiness can perform such a role; an Ethics+ approach provides the mechanisms to deliver this throughout the lifecycle of biobanking and other human health research.

It would be futile to attempt to offer a single model for what Ethics+ might look like across a range of contexts. But, we can identify the foundational elements of the approach:

1. Ethics+ draws us back to the strengths of bioethical reflection and the importance of sound ethical judgment;
2. Ethics+ requires – and reinforces – the need to articulate and pursue the underlying values at stake;
3. Ethics+ is more akin to governance processes than some pseudo-regulatory or quasi-legal framework – in this sense it must be designed to add value and not simply replicate regulations found elsewhere;
4. Ethics+ involves a range of actors and stakeholders, and perhaps most importantly, it requires engagement of those actors in the deliberative and reflective processes – mere compliance is no longer king;
5. Ethics+ probably requires stewardship of these processes, that is, trained actors who can support and facilitate the deliberative and reflective processes (for a fuller argument on the importance of regulatory stewardship, see: Laurie et al. 2017).

To return to the example at the beginning of this article, I suggest that the UK Biobank model is an instance of Ethics+ in action. Its Ethics & Governance Framework articulates key commitments and values that underpin the whole operation of the resource – from set-up, recruitment, management and access. Its Ethics & Governance Council acts not only as a critical friend, but as an ethical steward: not dictating what UK Biobank ought to do, but supporting UK Biobank's ethical reflections and deliberations towards its own decisions. Examples of the way in which UK Biobank has been responsive to processual governance, include:

- The revision of its no-feedback policy for imaging, as discussed above;
- The revision of the EGF after discussion with the EGC to make clear that information technology limitations meant that not all details of participants could be erased on withdrawal;
- Engagement with publics on controversial possible applications to use UK Biobank, such as for cloning, pointing out that wider legal regulatory mechanisms would render such applications unlawful.

Conclusion

This article has suggested that the relationship between law and ethics in biobanking specifically, and human health research more generally, requires reassessment. It has been argued that the respective strengths of these domains of public life in guiding human action have become blurred to the possible detriment of the research endeavour. By advocating a processual approach to governance – in contradistinction to procedurally-driven regulatory mechanisms – the article offers a model of Ethics+ governance that can reorient the oversight of health research towards the complementary and crucially important contributions of bioethics.

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