

Liminal Spaces Workshop: Regulating for Uncertainty

1-2 February 2018: Wellcome, London

WORKSHOP REPORT

WORKSHOP DESCRIPTION

Transformation and process towards the generation of novel insights, treatments and interventions are the driving forces behind productive research. Regulatory approaches in health research often tend towards categorisation of activities (e.g. research versus treatment) and objects (e.g. tissue versus data). In practice, however, boundaries used to delineate these activities and objects can become blurred, revealing numerous grey areas of ambiguity, overlap and uncertainty. Ultimately, this can lead to ‘regulatory compression’, limiting the flexibility necessary for conducting research and the recognition of experiences of all key actors involved. The risk is that in our desire for categorisation, certain activities, objects and the experiences of key stakeholders will be ‘lost’ in between regulatory spaces which are either unaccounted for or more nuanced than pre-existing regulatory approaches suggest. This workshop sought to bring together a host of stakeholders involved in areas of regulatory uncertainty in order to identify how we might better understand these dynamics within and across regulatory spaces and actors. The two-day workshop was organised around three core areas of investigation:

1) **Activities:** Different research-related activities correspond to distinct regulatory regimes but current processes can fail to account accurately for areas of overlap between activities. This can generate needless complexity and confusion. Overlaps are particularly pronounced in the context of (1) global health emergencies (Session Three), generating issues about compressed regulatory ‘time’ and (2) treatment, research and innovation (Session Five), giving rise to questions about regulatory ‘space’, and most particularly which regulatory space or spaces should be used.

2) **Actors:** Sites of uncertainty must be navigated by different actors within the health research setting (Session Two). Where boundaries become blurred, duality of roles are common but not unproblematic, for example the clinician/investigator, patient/participant. Further, the roles and responsibilities of, for example, RECs, regulators and regulatory stewards (Session Six) in assisting treatment and research communities in navigating grey areas must also be assessed. Who leads these actors through these sites of uncertainties, and what are appropriate examples of good practice?

3) **Things:** In addition to the regulation of activities, we seek to regulate the use and development of objects, which can themselves become sites of uncertainty not only because of ambiguity around their status’, but also because of their potential to act as agents of transformation of human experience,

well-being and practices more generally (Session Four). This theme examined the ways in which we seek to categorise different regulatory objects, the consequences of doing so, and asked whether we might find better ways of accounting for the transformative nature of regulatory objects, i.e. does it make a difference whether an object is ‘medicine’ or ‘embryo’, ‘device’ or ‘product’?

OBJECTIVES OF THE WORKSHOP

- Identify the dynamics in play in different sites of uncertainty in health research regulation
- Consider how different actors deal with scientific, regulatory, ethical and legal uncertainty and, depending on the context, guide others through these spaces
- Reflect upon how we might achieve streamlining, clarity and simplicity in governance whilst embracing complexity, the need for flexibility, customisation and proportionality
- Understand how we might more accurately account for grey areas in regulation
- Ask how effective, or otherwise, is the strategy of law in regulating ‘things’ and what might be missed if we overlook the human experiential element of the regulatory process itself
- Explore what it means to regulate for uncertainty, and consider how we can do this better.

PARTICIPANTS

Liminal Spaces Team: Graeme Laurie (PI), Edward Dove, Isabel Fletcher, Agomoni Ganguli-Mitra, Catriona McMillan, Emily Postan, Nayha Sethi, and Annie Sorbie. (All: University of Edinburgh)

Participants: Stas Birko (McGill University), Roger Brownsword (King’s College, London), Sarah Devaney (Manchester University), Marie Fox (Liverpool University), Nils Hoppe (Leibniz Universität Hannover), Matthew Hunt (McGill University), Isabel Karpin (University of Sydney), Ann Kelly (King’s College London), Aisling McMahon (Durham University), Peter Mills (Nuffield Council on Bioethics), Jose Miola (Leicester University), Jonathan Montgomery (UCL), Mary Ford Neal (Strathclyde University), Mike Parker (University of Oxford), David Porteous (University of Edinburgh), Rachel Smith (MRC Regulatory Support Unit), Paul Stenner (Open University), Marc Turner (University of Edinburgh), Nayeli Urquiza Haas (University of Kent), and Heather Widdows (University of Birmingham).

WORKSHOP SUMMARY

Session One - Welcome and Presentation of DELPHI Study

Graeme Laurie opened the workshop by reminding participants of the overarching goals of the Wellcome funded project, 'Confronting the Liminal Spaces of Health Research Regulation' (Liminal Spaces). These are to reimagine regulatory spaces relating to health research by challenging the creation of regulatory siloes and categories, as well as the role of law in creating and perpetuating the same, and by exploring the experiences and processes of regulation itself. This workshop sought to build on pre-existing contributions from the team, including a 2017 workshop on empowering actors in regulatory spaces and conceptual work on regulatory stewardship.

Stas Birko presented the preliminary findings of the Liminal Spaces Delphi policy study. This was a three-round participant-led exercise commissioned by the team that sought to explore a group of expert stakeholders' perspectives on current issues related to health research regulation and to provide a forum to understand consensus and divergence in the field. The initial questionnaire asked three sets of questions about: the operation of existing regulatory frameworks; how to regulate complex or novel areas of health research; and stakeholder engagement. The LS team analysed these answers and used them to develop two further rounds of questions asking for more detailed responses on a range of topics including instances of best practice in research regulation, the definition and management of risk, ways of achieving regulatory efficiency and responsive regulation, the responsibilities of regulators and researchers, the role of public interest criteria, and how public engagement should be undertaken. A detailed analysis of these results will be carried out by the team in the next few months, however, it is already evident that, despite the absence of consensus in these answers, on no topic were two clear camps of opinion observed to emerge.

Session Two - Regulating for Uncertainty: Theoretical Concepts

Peter Mills - Hypotheses and Ecstasies: the Possibilities of Ethical Governance in Biomedicine

Peter considered the regulation of health research practices and the processes of knowledge production that often stand outside the regulated order. He suggested that knowledge production may take place across both spatial distinctions and temporal change, and that these introduce thresholds.

Themes and Questions

What are the contributions and limits that theory can bring to practice?

What do moral debates which engage people beyond institutional and regulated settings bring to our understanding of regulatory processes themselves?

The ways in which regulatory activities and particularly knowledge generation are structured create regulatory silos and may perpetuate a lack of overall responsibility.

How might we reconceptualise the spaces between development and deployment of technologies?

There are inherent risks in offering spurious legitimacy to laws which were never designed to regulate certain technologies.

How do we know when law needs 'refreshed' versus when we need new law?

However, where there is uncertainty, traversing these thresholds is problematic because the next step is often under determined. He problematised the regulated spaces of biomedical research, characterising them as overdetermined (confused), underdetermined (ambiguous) or contradetermined (blocked). Through various examples relating to genome editing, Peter considered three kinds of thresholds: (1) between basic and applied research; (2) between jurisdictional (normative) spaces (and "organised irresponsibility"); and (3) between academic and clinical spaces, and the challenge of what to do with ecstatic knowledge. Peter highlighted the disruptive 'delaminating' effects of these kinds of thresholds at which the divergent interest perspectives of different actions may 'delaminate'. He contrasted the descriptive space of science and the normative space of ethics. He proposed that the latter may have role to play in revisiting the normative aspects of regulation, particularly with respect to: the orientation of knowledge production; the integrity of research practices, and the demarcation of jurisdictional territories.

Paul Stenner - On Liminal Affective Technologies (LATs)

Paul considered the differences between spontaneous and devised liminal experiences. The former 'happen to us' whereas the latter are self-generated using devised, aesthetic, ludic and sacred practices or rituals. He suggested that LATs that operate at the thresholds between states, spaces or relationships and can help us to potentialise transformation when change is needed but we are unsure as to what it should look like. Paul used the example of the work of organ donation teams as practices that seek to manage tragic, chaotic and transformative circumstances and decisions. Here he also introduced the contrast between transitions that are 'pivotal', maintaining positions and relations, and those that are liminal and disruptive. The consent process in such a case is the LAT in question. LATs can serve to dissolve structural expectations and precipitate transformative liminal experiences. Where law seeks to impose structure in the face of uncertainty, LATs may prepare us for, or facilitate transition through, a lack of structure. The LAT can guide us through otherwise uncertain and unstructured experiences.

Session Three - Global Health Emergencies

Mike Parker - Embedding Ethics in Research in Global Health Emergencies

Mike considered the challenges associated with 'anticipatory' mechanisms of the regulation of ethical aspects to research, including guidelines and ethics review. He asked how can we navigate the clogged spaces that give rise to overlap, gaps and conflict especially during global health emergencies (GHEs), which can test established

Themes and Questions

How does ethics work together with regulation to prepare for uncertainties?

It is important to delineate ethics and ethics review; moral craft v regulatory process.

What can ethics do that law cannot do? And vice versa?

Ethicists can perform dual roles as disruptors and facilitators in relation to the interpretation of guidance.

How can law be sufficiently responsive in an emergency context?

How do we offer readily available ethics support and advice without adding extra burdens?

What can we learn from the GHE context that will help us in regulating other sites of uncertainty?

When do emergency norms become the new norm(al)?

Liminality can in turn be viewed through the lens of opportunity.

approaches to ethics. In part, this is due to: the inherent uncertainties associated with GHEs, the nature of research and the increasingly international nature of research collaborations. Additional complexities arise when we consider the various technological developments in the ways in which we conduct research. Mike suggested that the ethicist can perform both disruptive and facilitative roles, leading us beyond guidelines: the ethicist can (helpfully) act as the grit in the oyster when it comes to thinking through what to do in the face on considerable uncertainty.

Ann Kelly – Emergency Regulations: Evidentiary Thresholds in the case of Ebola

Ann explored how the tensions between the humanitarian imperatives of disease control and regulatory apprehensions of risk played out in the accelerated development, testing and licensure of Ebola diagnostics. Through the notion of the ‘evidentiary threshold’, she traced the normative and technical contours of the emerging paradigm of emergency research and development. Important questions were raised around the commitment to data sharing, lack of cross-validation and downstream challenges of gaining access to, and testing of, samples. These issues are compounded by regulatory ambiguity, lack of harmonisation, differences between minimum thresholds for approval versus deployment, and call for convergence between national regulatory structures. There can often be a disjunct between approval mechanisms that support and promote product development in the emergency context and the cross-over into the non-emergency context whereby access or further use is denied, blocked or subjected to entirely different, stand alone, regulatory paradigms.

Matthew Hunt – Ethics and Experimentality in Humanitarian Innovation

Taking the ‘innovative turn’ as evidenced by the 2010 Haiti earthquake as a starting point, Matthew charted the processes involved in the humanitarian innovation movement (recognition - ideation - development – implementation - diffusion). He suggested that efforts to innovate ought to be assessed with due regard to risks introduced, altered relationships, the other approaches which may be displaced and fit to the humanitarian setting. He argued that considering humanitarian innovation as occurring in a liminal space could be of value. Such a framing of innovation can help to foreground ethical responsibilities of actors involved in humanitarian innovation, ultimately leading towards a value-sensitive humanitarian innovation. Liminality is often provoked by a chaotic, rupturing event. Liminality both recognises the breakdown of pre-existing structures and the need to lead people through the disruptive liminal experience. Reflecting Paul Stenner’s comments on liminality as opportunity, Matthew offered concrete examples of valuable innovations arising from chaos.

Themes and Questions

How do we regulate ‘things’ when we do not know what they are and how do we differentiate this from not knowing how to regulate?

How do we identify where invoking the concept of liminality might be useful and where it might rather serve to obfuscate or defer important questions and commitments that ought to be exposed?

To what extent can law be responsive to relational value and status?

A role for liminality is in challenging the categorical nature of legal thinking itself (and in this respect the law might be usefully distinguished from regulation).

How can we generate a legal system which addresses transitional and intergenerational notions of harm?

Liminality is about more than spatial or temporal ambiguity; the idea of transformation is a key aspect of regulating at the margins.

Session Four - Margins and 'beings'

Mary Neal – What Kind of Thing is a Foetus?

Mary posited the human embryo/foetus as a liminal or marginal being and that this presents challenges for regulating activities affecting these entities, for example in calls for 'less law' pertaining to the termination of pregnancy. She suggested that when we purport not to know what an entity is, we marginalise and 'other' it. This other-ing of the human embryo/foetus is perpetuated not only by the law's reluctance to commit to saying what these entities *are* – opting instead to talk about what they *are not* (e.g. that they are "not nothing" (*St George's Healthcare NHS Trust v S* [1998] EWCA Civ 1349)) or refusing to arbitrate their personhood (e.g. the Warnock Report (1984) and *Vo v France* [2004] ECHR 326) – but also by the law being in thrall of the ideal of the rational, liberal subject. We treat the embryo as a 'gothic' object of fear and pity. Mary proposed that these positions need to be challenged if the law is to deal justly with the embryo/foetus. This means, first, acknowledging what we *do* know about human embryos and foetuses, amongst which she included that they are: human, alive, vulnerable, relational and challenging beings. And, secondly, we need to recognise that the ideal liberal subject of law is itself a fiction.

Isabel Karpin - Liminality and the pre-conceived embryo

Isabel spoke about the physical and temporal liminality that is implied by attention to, and attempted protection of, the 'pre-conceived embryo' in debates about the intergenerational transmission of harm. These debates follow from still-contested hypotheses about the epigenetic effects of the uterine environment. Specifically, it was suggested, this raises concerns about the framing of women's own health (including mental health), behaviour, environment, and experiences (for example of abuse) as potential risks to or "assaults upon" the health and wellbeing of future persons. This, in turn, raises questions about attribution of responsibility for these potential harms. This introduces several ambiguous or liminal entities: the future embryo as a concrete entity already under protection; women as "perpetually pre-pregnant" beings; and women's bodies as potentially toxic environments. Women are re-constituted as hostile environments and as conduits, rather than victims, of harm. We could say 'It was proposed that we need a radical revision of law that does not purely rely on claims of future harm, nor that perpetuates or indirectly promotes the above views of women. It is important to ensure that legal responses are nuanced and not merely driven by any scientific claims about future harm. The value of a liminal analysis lies in the fact that it draws attention to the experiential, transitory, processual, relational and uncertain aspects of future relationships.

Marie Fox- Animals Out of Place: the Care Home as a Liminal Space

Marie discussed the valuable role of companion animals in care homes. She highlighted the potential for animals as regulatory objects to move and transition between different spaces, and focused on the uncertain status of companion animals: are they simply 'pets' or 'family members'? The question posed was whether liminality can

help us to think about more responsive approaches from the law to companion animals. **It was proposed that we may see care homes as liminal spaces and 'beastly spaces', between institutions and homes: somewhere that is both 'home' and 'not home'. The spaces and the entities that occupy them are subjected to multiple liminalities.** In particular, companion animals, such as pet dogs, may be seen as liminal and 'uncanny' beings that sit between object and subject, transcending mere thing-hood. When their companion animals are not recognised as integral part of residents' lives and separated from them or destroyed, their owners' interests are non-trivially harmed. This poses the question of how such separations might be prevented. These animals are not regarded as family. But nor does a property model seem suitable, as people may come to see them as persons rather than objects. There may be value, therefore, in recognising the liminal status of these animals. It was proposed that we might constitute a companion dog in law, and thus broaden the capacity of the law to protect them, by respecting their relational status.

Session Five - Treatment/Research/Innovation

Sarah Devaney - Regulating for Uncertainty: Reputation to the Rescue?

Sarah asked whether research scientists' concerns for their reputation could be used as a regulatory tool to increase certainty from the perspective of regulators. She employed the example of the world's first 'three-parent baby' to illustrate some of the challenges to the legitimacy of regulators in the context of innovation. In particular, recognition-seeking behaviours can lead to scientific fraud. She asked how we might encourage scientists to behave in ways which are not 'legitimacy-harming' and which can achieve a level of certainty. Using the example of Jennifer Doudna's work on CRISPR Cas9 biotechnology, which involved extensive public engagement (in response to fears over science outpacing regulation), Sarah argued for the co-opting of publics and funders into the regulatory endeavour through dialogue, moving beyond traditional 'naming and shaming' approaches. She argued that a preventive and prospective approach will achieve a greater level of certainty for regulators.

José Miola - Innovative Treatments: The Spaces In-Between and 'Bad Bargains

José considered the current swathe of 'right to try' legislation in the US as an example of the role of the law as anti-regulator, i.e. where the law is actively employed to subvert regulation. Noting that while right to try rhetoric is framed around freedom of choice and the free market, he suggests that a more accurate framing is 'freedom from (state) interference'. The reality is that patient access to drugs come at the expense of legal and regulatory protections,

Themes and Questions

In what concrete ways can regulators address/affect nudge in order to increase certainty and predictability?

What are the lessons we need to carry forward in achieving a balance between exercising discretion, encouraging innovation and protecting against risks?

Notions of choice and conceptualisations of patient as consumer can undermine the law's ability to protect patients.

The law can be seen as a 'trickster' and anti-regulator, being used to subvert regulation in the context of right to try.

for example lack of reporting requirements. José contrasted the US position with the rhetoric in the *Montgomery* Supreme Court decision, problematising the reference to patients as ‘consumers’. He suggested that such a framing undermines the laws ability to protect us against fraudulent activities. In concluding, he suggests that when considering regulatory structures, we should resist this notion.

Marc Turner - Tensions between Practice of Medicine and Pharmaceutical Regulation in Advanced Therapeutics

Drawing on examples from advanced therapeutics such as synthetic tracheas and gene therapies, Marc highlighted the difficulties encountered in practice in distinguishing between the practice of medicine and medicinal products. He suggested that these categorisations are beginning to break down when we consider the wide spectrum that spans from minimally manipulated products across to combined therapies. In working through the value chain of such products, he stressed that products that are finally developed are often different to those initially administered. A particular site of complexity lies in the fact that advanced therapeutics continue to ‘evolve’ in the patient, unlike traditional medicinal products. This is an area where the labelling of law – its creation of discrete silos of regulation – breaks down, or at least is seriously and serially challenged by the experiences of both the researchers in producing such therapies and of the patients who seek to benefit from them.

Session Six - Regulatory Responsibilities

Rachel Smith - Supporting the research community through regulatory change: some practical aspects

Rachel used the forthcoming General Data Protection Regulation (GDPR) as a case study through which to explore some of the difficulties encountered by the MRC Regulatory Support Centre in supporting the research community through periods of transition. She emphasised the importance of early consultation with researchers in order to understand their concerns over the potential impact of the new regulation and the need to provide appropriate guidance and training to support the research community. A particular challenge lies in the provision of effective and timely communication, further complicated by the fact that goalposts are constantly shifting, multiple actors are involved in interpreting and developing policy and complexities can lead to rumors and organisational angst. She stressed that collaboration and engagement

Themes and Questions

Traditional categorisations of activities and things (e.g. medical practice and medicinal products) are becoming increasingly blurred

How do regulatory regimes account for products which evolve so much between initial administration and final development for market?

Supporting the research community necessitates early consultation, identification of areas of confusion, training and consistency in key policy messages

Challenges to supporting the research community arise out of complex and constantly shifting regulatory frameworks

Liminality is most helpful when it challenges how lawyers and regulators think about the processes of regulation and also what is the experience of regulation, for both regulator and regulatee alike.

Regulatory temporality is an important issue that does not receive much attention, that is, *when* should we regulate, when should regulators act or engage or communicate, and when should they do nothing?

are key to minimising duplication, maximising reach, steering interpretation and focusing impact. Time was also of crucial relevance: knowing *when* to engage with a regulated community can make all the difference in securing regulatory uptake and buy-in.

Jonathan Montgomery - 4 basic things: why the regulatory system is broken and what we should be doing about it

Jonathan characterised the current model for regulation of health research as one which is at breaking point. For example, boundaries between disciplines are increasingly meaningless (e.g. research versus audit, health care versus social care); the assumed separation between researcher and participant has transformed into a relationship of co-production, and the power of familiar professional ethical codes is increasingly diluted. He posited that those engaged in research (e.g. engineers, statisticians) are not bound into the value system upon which the (medical) regulatory system is based and in turn, this gives rise to potential clashing of value systems. In claiming that innovation can only be weakly regulated by nation states, he suggested that the value of regulation needs to be promoted. This would assist us in achieving a balance between encouraging globalisation and accounting national differences whilst simultaneously gaining a competitive advantage. In his final example, Jonathan highlighted that there seems to be collective amnesia about the history of the provisions in the Oviedo Convention regarding prohibition of germline modifications and the fact that these were only ever intended to be provisional. This highlights the spurious certainty of instruments that were initially drafted for one purpose, and to which we subsequently built-in new objects of regulation.

Roger Brownsword - Three levels of regulatory responsibility

Roger identified and considered in turn three distinct lexically ordered levels of regulatory responsibility and considered what 'stewardship' necessitates in relation to each level. Primary responsibility relates to maintaining and preserving conditions of the commons: regulators everywhere are bound by non-negotiable responsibilities, which Roger argued hold in all places, even if specific regulators do not recognise them. Secondary local, more parochial responsibilities account for plurality, they distinguish what distinctive values are and ways of respecting them and ensuring their protection. Communities should be able to articulate and privilege their own sets of values. Tertiary responsibilities lie in balancing (parochial) legitimate interests. Roger explained the difficulties associated between determining which level of responsibility regulatory issues might fall under. For example, in the context of data processing, the question arises of whether privacy would be viewed as a primary (fundamental) right or rather one consideration amongst many competing interests within the data protection framework.

EMERGING THEMES AND QUESTIONS

- Temporal regulation: when and how do we determine when to (re)visit a topic socially, ethically and from a regulatory perspective?
- How do we support actors in emerging from phases and processes which are temporally limited (e.g. the GHE setting)?
- When new technologies emerge, when do we attempt to fit the new technology into existing law or looking to new modes of regulation.
- How do we regulate things/activities/actors that do not already fit into pre-existing categories, and how do we differentiate this from not knowing *how* to regulate them?
- Relatedly, how can law capture and reflect the blurriness of the subject-object distinction when regulating some 'things, but also capture the importance of relationships within that?
- Consent is the start of a new process of becoming and implies a new sets of new assemblages; what are the implications for consent in health research regulation, seen in these terms?
- Can regulatory nudge be conceived of as both an option and as a way of (1) leading regulatees through regulatory space and (2) persuading them to remain in regulated spaces?
- How can we account for projects that do not progress from conception to realisation? How can the current ecosystem capture this?
- How do we facilitate and advance productive debate on morally sensitive subjects where regulatory regimes are already established, e.g. embryo research?
- Is it 'new' regulation per se that causes anxiety amongst researchers/regulates, or is it types of regulation or how they are developed/implemented?
- On whom do responsibilities fall to help regulatees navigate (i.e. make sense of and work through) regulation? Might these responsibilities be shared amongst regulators, regulatees and third parties?
- How do we determine when regulatory experts are in fact 'pseudo-experts', purportedly offering advice to work through complex regulation (e.g. GDPR) but emerge as 'tricksters', and in turn, what is a suitable regulatory response, if anything?
- Is there a risk of invoking the concept of liminality so as to obscure our normative commitments, in a way that does not serve productive debate? Might 'strategy' be a more useful conceptualisation?
- How can we make the most of periods when existing structures and order are disrupted, so as to achieve processes or outcomes that respond to new and shifting needs – productive disruption?
- What value is there in exploring concepts such as "the virtuous researcher", especially when confronting the risks of the "mechanistic approach of ethics committees"?