5. Operationalizing 'next-generation' health research regulation—what is happening in practice?

I. INTRODUCTION

The principal aim of this and the following chapter is to engage with the empirical data collected from the interviews and observations and, coupled with the findings from the document analysis, make sense of them through an anthropology of regulation approach, as outlined in Chapter 4. In this chapter, I explore what happens in REC meetings, consider the operationalization of 'next-generation' health research regulation (particularly in light of the twin aims of protection and promotion), and investigate the procedures and substance behind risk-based regulation. I do this by querying whether risk-based regulation is actually being practised by RECs and the HRA, and more fundamentally, by querying the nature and function of the interactions among RECs, researchers, and the HRA. Throughout, I draw on the implications of space and time in the process of research ethics review, signifying the contribution of liminality to the normative discussion that follows in Chapter 6.

In what follows, I present three themes (subdivided into categories) that emerged from the data. These findings consist of evaluative statements based on an overall assessment of the raw data informed by an anthropology of regulation. I rely on direct quotes or extracts of fieldnotes where they specifically enrich the analysis. Given the wealth of data in my notes, however, I cannot do this everywhere. A significant category within the third theme—regulatory stewardship and its connection with liminality—will serve as a bridge to Chapter 6, which, taking up the normative dimension of anthropology of regulation, provides recommendations for refining the health research regulatory framework.

II. THEMES

Each of the three themes focuses on different aspects of regulation and transition. Combined, they paint a picture of a health research regulatory system that both REC members and regulators support, but do not always praise. For REC members and regulators, the current system demonstrates vast improvement in the last decade. To this end, most members were supportive of the HRA's efforts to further centralize research ethics and create common standards to improve quality and consistency, as well as efficiency. At the same time, however, many REC members were also critical of certain aspects within the system, including the at times fraught relationship between the HRA and its equivalent bodies in the devolved administrations, and—perhaps surprisingly—between the HRA and RECs themselves.

My findings suggest that research promotion is *not* a 'new' twinned role for RECs—some additional primary responsibility only recently foisted upon members—but, the findings reveal that the practices of REC members vary greatly in how this role is both conceptualized and instantiated. In enacting their regulatory roles, whether for risk/burden-benefit analysis, assessment of the consent process, or legal and scientific checks (itself a questionable role), REC members and regulators demonstrate the value of stewardship—most notably expressed through the work of REC Managers, REC Chairs, and Scientific Officers—to set an example for others to follow, and guide REC members and researchers alike across the stages of the research application process. Within this latter observation, we uncover key insights into the liminal spaces RECs occupy and the potential role they may play across various thresholds of the research lifecycle, including those beyond the current *ex ante*-dominant positioning of ethics review.

The following subsections investigate three themes, namely: (1) the 'black boxes' of ethics review; (2) regulatory connectivity; and (3) regulators as stewards. In light of the methodology described in Chapter 4, we will find that elements of anthropology of regulation appear in each of the three themes identified.

1. Regarding the first theme of 'black boxes' of ethics review, anthropology of regulation helps frame the regulatory behaviour of RECs as an instance of internal flexibility, where individual and group behaviour impacts and indeed helps shape a regulatory space wherein RECs and researchers alike explore and deliberate the 'ethics' of a research project. Liminality, in turn, draws our attention

to rituals and how they play a crucial role in regulatory coordination. The rituals in ethics review serve to organize the REC's actions and reinforce its authority, but they also drive collaboration and coordination with other actors, particularly researchers.

2. Regarding the theme of regulatory connectivity, anthropology of regulation invites us to consider the influence of law, science, and ethics in REC work. Rather than viewing each of these as disciplinary and regulatory 'boundaries', we are better placed to view them as connected regulatory spaces that call for guidance to work through and across each of them. Law, science, and ethics are all wrapped up together in the making of an ethics opinion.
3. Finally, regarding the theme of regulators as stewards, anthropology of regulation suggests that particular actors can serve as 'masters of ceremony' in guiding other actors (most often researchers and sponsors) through stages and thresholds of regulatory processes, where uncertainty often is paramount. This last theme therefore teases out the crucial finding that actors within and connected to RECs serve as 'regulatory stewards' who help guide researchers, and their applications, across stages of the research lifecycle, and that the HRA as a managing regulatory authority can take a leading role here.

I now proceed to explore each of the three themes, commencing with the 'black boxes' of ethics review.

2.1 The 'Black Boxes' of Ethics Review

2.1.1 Learning by observation

As earlier chapters have underscored, much is unknown about how REC members learn to 'do' ethics reviews and what actually happens in the course of their work before, during, and after a committee meeting. As anthropology of regulation aims to investigate the nature of regulation and the behaviours and experiences of actors within a regulatory space (or spaces), and the ways in which they are affected by, and in turn affect, regulation, I was interested in understanding how people learn to become REC members and perform the regulatory task of assessing the ethics of research. I was interested in knowing whether REC members felt their knowledge—or indeed expertise—was formed primarily by formal training sessions and regulatory documents, or by the experience itself—learning by doing, in other words.

By and large, REC members felt that they learned how to 'do' ethics reviews by observing other REC members in action. They watch, listen,

and learn, but what REC members pick up is not necessarily carbon-copied into their own particular ways of doing committee work. Their observations are individually interpreted and subsequently manifest themselves in unique ways based on their own values, experiences, and expertise. Training, such as the mandatory induction for new members, provides a cursory overview of research ethics and points them in the right direction for additional resources if they are uncertain about specific areas, but the actual practice of ethics review—the process of working through applications; adopting the rituals, mannerisms, and jargon during meetings; evaluating forms; questionning researchers face-to-face; and writing up reports—is learned by observing other members who have obtained this experience. It is through this that members come to contribute 'effectively' and produce a culture of ethics review. As one REC member explained:

> I wasn't expected to contribute for the first few meetings—so if I wanted to I could have done—but it was mostly, 'You're here to learn about how things operate and what sorts of things we're going to be discussing', and then just picking it up from those meetings. […] The best way to learn is by listening to what the other members come up with. (P6)

If REC members learn by observing other members and also individually interpret applications based on their own values and experiences, what might the process of an ethics review look like? How might one describe it? An HRA regulator described ethics review as a 'black box' where the process of review itself constitutes the outcome:

> To some extent you just have to sometimes, I think, look at the RECs as a black box and you just say, 'Well, that's how we have decided in this country and across the world to deal with that ethical decision making.' That's it, that's the black box—it's up to 18 people around a table discussing it and out pops the opinion. And it's a bit of a difficult one to get into that black box and mess around with it. It's almost that the process is the ethical decision. We've just decided that's the process and what pops out and we'll live with it. You know, you can train the people who are inside the black box and do everything you can, but I think to some extent this is probably as good as it gets when you get [86] committees with up to 18 people sitting around a table making ethical decisions. (P1)

It was the reference to RECs as a black box and the *process* of deliberation as constituting the ethics opinion in this first interview that propelled me to look more closely inside RECs. Does the practice of ethics review align with what the regulations would suggest happens, or should happen? Do REC members have any sense of what other RECs

do, any curiosity about it, or any desire to know if they are being 'consistent'? As opposed to a singular black box, could there be a multiplicity of unconnected black *boxes* operating in fairly splendid isolation—and yet with still a fair degree of homogeneity in culture? How exactly does the process of ethics review itself constitute an opinion—not input and then output, but input *as* output, and arguably process as product?

2.1.2 Ethics review—peering inside the black boxes

The HRA's guidance document, 'Information for Potential Research Ethics Service Committee Members', outlines a process of ethics review in RECs that focuses on the utilitarian calculus of risk-benefit, a robust consent process, and adherence to the REC SOPs and relevant guidance and legislation.[1] The evidence from my research suggests that RECs follow this guidance. A great deal of effort and time at meetings is dedicated to three areas: (1) ensuring that the consent process is robust, such that participants are fully informed of all material issues in a Participant Information Sheet (PIS) and are able to make a voluntary decision to participate in a project; (2) ensuring that the burdens and risks to participants are minimized as far as possible, and risks to the researchers are minimized; and (3) ensuring that there is methodological robustness to the project, that is, that 'the science is right' (this focus on scientific quality is discussed further below).

Within these three areas of focus, all five RECs I observed approached research projects liberally. As one REC Chair explained: 'I think sometimes we have to remind ourselves that if the risks to the participants are minimized as far as possible then that research should probably be allowed to happen' (P3). The prevalent view that I observed is that provided risks are outweighed by potential benefits (or there is a 'fair balance' between risk or burden and potential benefits), and participants are provided with all material information during the consent process, then the choice to participate should be theirs to make, not the REC's. A member elucidated this liberal approach as follows:

> sometimes you have to be careful not to be paternalistic in that actually … well, so long as people have a choice, they don't have to do the study, and if they don't like the fact that they're not going to get paid or they're not going to get travel expenses, we might suggest, 'Well, it would be nice if you could

[1] Health Research Authority, 'Information for Potential Research Ethics Service Committee Members' <www.hra.nhs.uk/documents/1025/standard-application-pack-rec-members.pdf> accessed 22 October 2019.

> pay them, but if you're not going to pay them then the person won't do the study.' There's a fine balance between thinking a participant hasn't got the brains to work things out for themselves and they have to be mollycoddled every step of the way. It's really hard to think of things that you just want to go: 'No, you can't do that.' (P8)

In REC meetings, ethical issues within the three areas mentioned above are transformed into questions of refinement, or what might be called technical questions (e.g. inconsistencies between the research protocol, PIS, or IRAS form; missing information in the PIS; clarification of the participant recruitment process; whether there will be continuation of the study drug after the clinical trial ends). Fundamental questions demanding meta-ethical reflection (e.g. the ethics of gene therapy; the ethics of 'me-too' drug applications) rarely manifested themselves in REC meetings. Instead, there was a cumulative gathering of information: members tended to reinforce other members' comments through adding their own, often in complementary ways. This may be a pragmatic matter driven by time and resource constraints. Or, this may be a matter of REC members thinking it inappropriate, or thinking themselves incapable, of engaging in deep ethical reflection or debate. After all, RECs do not function as a bioethics council (such as the Nuffield Council on Bioethics) where there are resources and an explicit mandate to deep dive into matters of ethical concern. Rather, RECs function more as regulatory event licensing bodies that individually evaluate and collectively deliberate on submitted documents and render a decision underpinned by standards, principles, and intuition. This reinforces legal scholar Carl Schneider's claim that the REC system 'is not an engine for abstract ethical thought. It is an agency *regulating* research',[2] and legal scholar Jonathan Montgomery's claim that a REC 'rarely engages directly in ethical reflection, but is concerned with ensuring compliance with established standards'.[3]

As such, to the extent that there is an underlying ethos guiding these RECs, it appears most strongly as liberalism and pragmatism. Each member is tasked with interpreting and applying ethical standards and principles (and to some degree, laws and regulations) to specific research projects. How these standards and principles are instantiated vary among individual members and, to some extent, among RECs. But, while the individual interpretations can vary, they are not limitless.

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[2] Carl Schneider, *The Censor's Hand: The Misregulation of Human-Subject Research* (MIT Press 2015) 107 (emphasis added).

[3] Jonathan Montgomery, 'Bioethics as a Governance Practice' (2016) 24 Health Care Analysis 3, 11.

In her ground-breaking empirical work on IRBs in the US, the historian Laura Stark invokes an 'ethics of place'[4] to denote the peer review model of IRBs—*institutional* review boards—that attaches ethics to a specific physical place—a particular building—rather than a classic code of ethics that attaches to an individual physician or researcher. Peering further into the 'black box' of ethics review in the UK, several key findings emerge that suggest NHS RECs, unlike their institutional counterparts in the US, symbolize an *ethics of space*. Ethics is attached to the REC within their meeting space at an NHS Trust hospital, Health Board, or hotel conference room, yet as a node within networks (RES, NHS, and others), theirs is also an ethics informed by a larger regulatory framework such that moral authority for a decision rests not just in the REC itself, but also in the institutional apparatus of the RES(s). As bodies that have become increasingly centralized, their independent 'room to roam' is still wide, but it is not infinite. Ethically appropriate research must fit within the personal sensibilities of REC members, as well as institutional sensibilities set by the HRA and equivalent bodies that prescribe boundaries of ethical (and legal) acceptability. Invoking an anthropologically informed view of regulatory practice by RECs, we find that the 'ethics' within research *ethics* committees is a proving ground of debate, deliberation, and negotiation, and a regulatory space that accommodates diversity, disagreement, and dissent across applications and across time.

Within this ethics of space, a common behaviour exists across RECs. Intriguingly, relative to each other, RECs are black boxes, existing in multiple spaces. Several REC members I spoke with perceived a top-down command from the HRA, while HRA regulators told me they perceived a collaborative ethics co-produced with RECs. Several REC members also perceived that they had little interaction with other RECs. Beyond the regional REC Chair meetings held twice a year (across regions in England), 'ordinary' REC members do not have common opportunities to engage with other RECs, and they do not seem to have much desire to do so. Yet, despite these black boxes existing between black boxes, there exists a surprising degree of group homogeneity in terms of approach and rituals. What drives this homogenous REC group culture across the different black boxes may be in part HRA standards driving consistency, but this can only be a partial explanation. Many of the rituals and routine performed by REC members are not simple

[4] Laura Stark, *Behind Closed Doors: IRBs and the Making of Ethical Research* (University of Chicago Press 2012) 83.

instantiations of HRA standards. Even if RECs maintain a relatively wide latitude in which to roam, they appear to roam in similar ways and in similar spaces. Even more intriguingly, elements of REC culture—interpretive flexibility, self-policing behaviour, sensitivities with regard to relationships with researchers—would ordinarily suggest heterogeneity, not homogeneity. What might explain this?

The ethics of space illustrates the symbolic importance of inviting various actors, such as researchers, into the black box of ethics review, and it illustrates how the physical dimensions of space impact on the processes of review. The space that is created is on the REC's terms, even if it may be part of the physical space of the NHS or another's community. For instance, a clinical researcher may be on her 'home turf', residing in the same NHS Trust hospital as where the REC meets monthly, but she must still face the black box by entering the conference room, presenting her research project before the members, and submitting to their judgement as the REC casts its opinion on whether her application is ethically acceptable. One might think that this is a recipe for adversarial conflict, driven by a desire for research promotion versus a desire for participant protection. Quite on the contrary, researchers invariably seem to submit to the REC and work together alongside them in moving the research application along towards ethical acceptance. Indeed, only once did I observe an overtly hostile situation where a researcher was unwilling to participate in the REC's ethics of space and overtly demonstrated an unreceptive attitude. The REC Manager later told me that this researcher had been to the REC several times before and had a bit of a 'reputation'. Even so, this hostile situation and ostensibly unfriendly relationship did not seem to have any bearing on the REC's view towards the research application. The outcome recommended by the Lead Reviewer and subsequently agreed by the REC as a whole was 'favourable with conditions'.

In sum, an ethics of space constitutes a connected network of RECs across the UK where cultural homogeneity is paramount. A researcher can submit an application in Southampton in the south of England or Aberdeen in the north of Scotland and is likely to experience a very similar ethics review (and a REC whose members are rather similar in demographic composition), even if the ultimate outcome may differ (e.g. favourable opinion versus provisional opinion requiring further information). RECs themselves may not be aware of how similar they are culturally. More than once REC members asked me how their REC 'compared' to the others I was observing, and whether I found any differences. As I responded to them, the differences are few and far between. Despite, or perhaps because of this homogeneity, there is a

strong desire by RECs, including REC Managers, to preserve the sanctity of *their* black box and ethics of space. As will soon be shown, initiatives by the HRA that try to improve the regulatory pathways for researchers can backfire if there is improper consultation with RECs. Specifically, the 'Ethics Officer' pilot, discussed later in this chapter, can be interpreted as an invasion of this ethics of space. Researchers who enter this space do not create tension, yet other regulators who enter into it can. The irony, then, is that in the present context, regulatory tension or failures exist between regulators, not between regulators and regulatees.

2.1.2.1 A liberal approach to risk and expected benefit The GAfREC state: 'The [REC] has to be assured that any anticipated risks, burdens or intrusions will be minimised for the people taking part in the research and are justified by the expected benefits for the participants or for science and society.'[5] Elsewhere, the GAfREC state that 'research can sometimes involve an element of risk, because research can involve trying something new. It is important that any risks are minimised and do not compromise the dignity, rights, safety and well-being of the people who take part.'[6] Specific guidance is not provided as to how this evaluation of anticipated risks and benefits is to be conducted, or how risk minimization may be done. As we saw in Chapter 4, this concerns scholars such as Annette Rid, who argues that 'frameworks for risk-benefit evaluations of biomedical research remain surprisingly vague'.[7]

Compared to Jan Federici Jaeger's ethnographic study of IRBs in the US, which found that '[m]ost of the time that an IRB spends on a proposal review is focused on identifying and deliberating about risk',[8] my findings suggest that RECs spend *some* time per application discussing risk, but it does not comprise a majority of the REC's meeting time. Moreover, to the extent that the risk-benefit or burden-benefit calculus is invoked in decision-making, a number of REC members tended to focus their discussion more on the prospective evaluation of burdens to participants (usually framed as 'mere inconveniences', typically of a temporal or financial variety) than risks of a physical, psychological, or

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[5] GAfREC para 1.2.2.

[6] ibid para 2.2.1.

[7] See Annette Rid, 'Rethinking Risk–Benefit Evaluations in Biomedical Research' in Daniel Strech and Marcel Mertz (eds), *Ethics and Governance of Biomedical Research* (Springer 2016) 153.

[8] Jan Federici Jaeger, 'An Ethnographic Analysis of Institutional Review Board Decision-Making' (PhD thesis, University of Pennsylvania 2006) 94.

social variety. Only on occasion were expected benefits of the research project discussed.

One Scotland A REC member agreed that, at least as far as her REC was concerned, the members look at 'the burden probably more than the risk actually. We do occasionally get quite risky looking things, but they're usually in people who are really not well, I mean, really end of life' (P12). This may be because many REC members feel that risks in most projects are in fact relatively minimal (even though they are not non-material as compared to Proportionate Review applications); that there is a high level of unambiguity and certainty in the risks present in most research projects (and thus they do not need to be assessed in any systematic way); or that the scientific aspect of risk assessment is beyond their scope (unlike, say, the MHRA).

Discussions of risk in REC meetings were often limited to their identification, that is, a listing of what they were as identified by both the researcher in the application materials and the REC members in their review of the materials. The majority of the time, this was done by the Lead Reviewer. Explicit risks, burdens, and benefits may be gathered from the IRAS form: question A22 of the form asks the Chief Investigator (researcher) to list 'potential risks and burdens' for research participants and explain how they will be minimized; question A24 asks about the potential for benefit to research participants; and question A26 asks about potential risks for researchers themselves. Non-explicit forms of risk, burden, and benefit may be drawn out in the HRA Ethical Review Form's question 3, which asks REC members to consider whether the risks to the research participant are proportionate to the benefits to the research participant and society. Thus, some risks and burdens are explicitly identified already by the researchers; others may be implied (i.e. drawn out by REC members in their review and discussion); and still others theoretical (i.e. remote) or unknown (i.e. risks or burdens that the REC cannot identify due to missing or inaccurate information).

Chapter 4 explored risk-based regulation, which can be defined as 'the prioritizing of regulatory actions in accordance with an assessment of the risks that parties will present to the regulatory body's achieving its objectives'.[9] Looking back at the elements listed in Box 4.1 in Chapter 4, risk-based regulation tends to encompass a broad sweep of risk assessment (or appraisal), risk management, and review, including scoping the various dimensions of a risk, considerations of framing (i.e. how different

[9] Robert Baldwin and others, *Understanding Regulation: Theory, Strategy, and Practice* (2nd edn, OUP 2012) 281.

stakeholders may have conflicting views concerning a risk), scientific risk assessment, and the broader social, institutional, political, and economic contexts that must be taken into account in risk-related decision-making.[10] RECs do provide written opinions and allow for appeals and at times engage in analogical reasoning, but they do not seem to follow specific rules governing particular aspects of the risk assessment process. As the legal scholar Lars Noah argues, risk assessment is a separate endeavour than burden or risk-benefit assessment;[11] the latter may not necessitate 'objective', scientific measurement so much as an intuitive balancing and effort to minimize (i.e. manage) risks that may manifest.

And indeed, in the full committee meetings I observed, RECs, and in particular REC Chairs, strived to enact a liberal approach in ethics review while avoiding a paternalistic stance towards risk. No member seemed wantonly unconcerned about risk; none would allow unfettered risks to be placed on participants. At the same time, though, the REC meeting discussions did not give me the impression that risk assessment and management were often the central focus. Members did not frame their approach to ethics review as a calculus such that their level of scrutiny of a research project was definitively determined by the level of risk it posed to participants. Rather, risk was discussed as part of a much larger whole of ethics evaluation. Commonly, risk was a matter to be made clear and explicit in a PIS, and for a potential participant to weigh. As a Scottish REC member explained: 'Nobody wants to stop research being done; we just want it to be done so the person being studied is fully aware of everything that's going to happen to them and to make an informed choice about whether they want to participate or not' (P18).

An example of this liberal approach can be drawn from my fieldnotes. As I was leaving at the end of one REC meeting, I stopped to chat with the REC Chair. I explained that I was interested in how issues such as risk are conceptualized and assessed by RECs. The Chair thought for a moment and said, 'I don't think this is really a philosophical issue; it's a practical issue. Most research is not at all risky. Where's the evidence that research is risky, beyond a Phase 1?' he asked. He then continued: 'Who's died from research? Some people have, but more people have died from unresearched care. Actually, if you look at the meta-analyses, taking part in Phase 3, Phase 4 research is neither good for you nor bad

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[10] International Risk Governance Council, *An Introduction to the IRGC Risk Governance Framework* (IRGC 2012) 8–10.

[11] Lars Noah, 'Deputizing Institutional Review Boards to Police (Audit?) Biomedical Research' (2004) 25 Journal of Legal Medicine 267.

for you.' Pausing a moment for further reflection, he then added, 'I wonder what health research regulation would look like if we considered research to be good for you.'

This liberal approach towards risk may work at some level to address the 'heterogeneity problem' raised by the legal scholar and bioethicist Michelle Meyer.[12] While RECs as a group appear to exhibit homogenous cultural and regulatory behaviour, scholars such as Meyer argue that individual research participants are heterogeneous in their preferences and other circumstances; thus the same research protocol will offer a different risk-benefit profile for different participants. Likewise, individual members of ethics committees assess risks and benefits based on their individual interpretation of their regulatory mandate to do so. Thus, REC members can engage in interpretive flexibility[13] when it comes to interpreting and operationalizing the regulations regarding risk-benefit assessment. As Stephens and colleagues demonstrate, interpretive flexibility can be a positive outcome in regulation. To overcome this heterogeneity problem, Meyer advocates greater private ordering whereby individual prospective research participants, rather than the ethics committee, decide whether it is reasonable for them to accept the risks of participating in a particular research project. In the REC meetings I observed, the liberal approach enacted a form of private ordering. RECs fulfilled their regulatory mandate to assess burdens, risks, and potential benefits, yet the most common occurrence for the REC was to insist on clear provision of risks (and honest portrayal of expected benefit) in a PIS. It was then for individual prospective participants (or their proxies) to decide whether it was reasonable for them to accept the risks of taking part in a given research project.

In my view, then, it cannot be said that RECs operate solely as risk-based regulators. Were they acting as such, we would expect to see, among other things, more objective forms of risk assessment (e.g. a system for assessing risks and scoring them, beyond Proportionate

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[12] Michelle Meyer, 'Regulating the Production of Knowledge: Research Risk-Benefit Analysis and the Heterogeneity Problem' (2013) 65 Administrative Law Review 237; see also Michelle Meyer, 'Three Challenges for Risk-Based (Research) Regulation: Heterogeneity Among Regulated Activities, Regulator Bias, and Stakeholder Heterogeneity' in I. Glenn Cohen and Holly Fernandez Lynch (eds), *Human Subjects Research Regulation: Perspectives on the Future* (MIT Press 2014).

[13] Neil Stephens and others, 'Documenting the Doable and Doing the Documented: Bridging Strategies at the UK Stem Cell Bank' (2011) 41 Social Studies of Science 791.

Review applications), management, and review; systematic improvement of decision-making processes based on new evidence and insights into potential risk; and allocation of resources where risk is greatest (e.g. more time and effort spent on gene therapy and Phase 1 clinical trials).[14] Instead, RECs' regulatory positioning towards research applications encompasses elements of risk assessment and risk management (such as communicating risks to participants), although the regulatory positioning extends beyond this. RECs regulate not on the basis of risk alone. The social and scientific value of a research project and its likely risks, burdens, and benefits are weighed by RECs; RECs decide whether burdens and risks to participants are ethically justified in light of, and reasonable in relation to, the potential benefits and scientific and social value of a project.[15] Thus, just as critical to RECs' operative deliberation is the *facilitation* of a context in which a fair choice is offered to participants whereby they can decide whether to participate in a project that presents ethically acceptable risks and burdens (as determined by the REC) and is likely to answer, or at least contribute to, the research question it purports to address. Moreover, the facilitation is directed not just to research participants, but also to researchers themselves, as I discuss further below.

This focus on facilitating participant choice aligns with the 2015 Nuffield Council on Bioethics' report on children and clinical research, which suggests that:

> the fundamental role of ethical review is to ensure that an invitation to participate in research would constitute a '*fair offer*' to children, young people and their parents, where the value of the research and its likely risks, burdens and benefits have been carefully weighed up.
>
> In focusing on the role of the REC in ensuring that research involving children constitutes a fair offer to children and parents, it is also important to recognise *the REC's second and equally important function: its facilitative role*, which arises in recognition of the essential social good of well-designed and well-conducted research. It is not an ethically neutral act to say 'no' to a research proposal that might potentially lead to better outcomes for children's and young people's healthcare.[16]

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[14] See e.g. OECD (ed), *Risk and Regulatory Policy: Improving the Governance of Risk* (OECD 2010).

[15] See also Jeffrey Cooper and Lindsay McNair, 'Assessing Research Benefits: Practical Ethicist' (2017) 12 Journal of Empirical Research on Human Research Ethics 191.

[16] Nuffield Council on Bioethics, *Children and Clinical Research: Ethical Issues* (Nuffield Council on Bioethics 2015) xxvii (emphasis added).

To preview the discussion to follow, here we begin to see one element of (ethical) research promotion. To the extent risk is assessed, managed, and communicated, RECs concern themselves with risk vis-à-vis its identification and mitigation (as set forth in the HRA Ethical Review Form) in a personalized (read: subjective) and socialized way (i.e. in the course of REC deliberation), but the scope of risk assessment and management is mitigated by a liberal, facilitative approach.

A final key finding within this theme is that different moral considerations apply to different types of research projects, in a twist to the risk-proportionate approach advocated by the HRA, which focuses on reducing the regulatory burden for research that presents 'no material ethical issues' for human participants. RECs approve research projects involving high-risk treatments for late-stage cancer patients (e.g. Phase 2 and 3 clinical trials), even though this means there might be known (quantifiable) risks associated with the treatment, or even unknown risks. They approve such projects on the basis that participants could accept the treatment with the full knowledge of the risks, and that *without* taking the treatment, they could well die rapidly. One reason for this is that, unlike a Phase I (first-in-human) healthy volunteer study, at least some of the risk-bearers may well also stand to benefit from the risks taken. As the ethicists Allison Ross and Nafsika Athanassoulis argue, 'while we normally tend to think of risks as something we want to avoid, research risks can be very attractive, especially for those whose last hopes for a treatment lie with the potential research benefits'.[17] In these situations, RECs do make ethical decisions knowing that there are associated high(er) risks. For them, the emphasis is placed on making that knowledge explicit and clear to the participants. The REC cannot speak on behalf of potential participants, but it can ensure that potential participants have accurate, up-to-date, and understandable information. From there, liberal autonomy seems to dictate: the choice is theirs to make.

This was evident in a REC review of a gene therapy trial that I observed. Here, unsurprisingly, risk discussions predominated. The REC's main concern was the balancing of safety and efficacy of the therapy. Following the initial discussion, three representatives from the research project were invited into the committee room, where the REC Chair began by asking them to describe their project. In a calm, cool, and well-spoken manner, the Chief Investigator described the proposed project. When the REC Chair then asked him about weighing safety and

[17] Allison Ross and Nafsika Athanassoulis, 'The Role of Research Ethics Committees in Making Decisions About Risk' (2014) 26 HEC Forum 203, 205.

efficacy, the Chief Investigator, with powerful rhetorical flourish, narrated a story about how participants understand risk better than we think. A potential participant once asked the Chief Investigator to sign his will before participating in a clinical trial, in case death occurred. The Chief Investigator, slowing his cadence at this point, said to the REC: 'And I didn't sign that will. And you know, I was glad not to because the man had planned to give everything to his girlfriend, and they then broke up six months later!' This drew laughter from the REC. 'He knew he was putting his life on the line,' the Chief Investigator continued. His point, of course, is that RECs should not assume participants cannot understand risks in research, much less substitute their judgement for a competent adult participant. If the information provided to them is honest and complete, the research should proceed. Following the face-to-face discussion, when the researchers got up to leave, the REC Chair beamed and said to the Chief Investigator, 'Thank you very much, that was fascinating!' After they left, the REC Chair looked around the table at his fellow committee members and said: 'What do you want me to do, team? He's quite persuasive, isn't he?' All agreed, and the outcome of this application was a 'happy provisional' opinion.

2.1.2.2 Pragmatic ethics The HRA disseminates ethics review guidance and policies driven by procedures; they do not offer guidance on how to conduct an ethics review by reference to substantive ethics. It is, as I discovered, up to REC members and key 'stewards' such as REC Chairs and Scientific Officers (as I further discuss below) to help guide the REC members towards an ethically informed decision. REC members were hard-pressed to pinpoint the ethical deliberative content in a committee decision. When asked to explain the process, they provided a procedural description that focused on the steps involved in working through the contents of the application form and attendant documents. Members reach an ethically informed decision of some type, but the decision-making process appears to be performed intuitively or pragmatically. Just as researchers rarely frame ethical scenarios in the moral philosophical language of deontology, consequentialism, and virtue ethics,[18] rarely was an ethical principle relied upon to justify a stance on an issue within an application. Members might have taken utilitarian perspectives or objective dignitarian perspectives when considering risk-benefit analysis (i.e. weighing risks against benefits, as the regulation

[18] David Johnson and Elaine Howard Ecklund, 'Ethical Ambiguity in Science' (2016) 22 Science and Engineering Ethics 989.

largely dictates, or suggesting a particular risk of harm could never be justified, regardless of any consideration of benefits), but none articulated them as such. Foremost, educated (and experiential) gut reactions and feelings drive ethical decision-making processes to render an opinion that seems suitable to and workable in the context at hand.

This finding accords with philosopher Mary Warnock's argument that 'morality cannot be divorced from sentiment'[19] and '[e]thical decisions cannot be taken without the examination of ethical feelings'.[20] Each REC member brings their own culture of moral reasoning to bear on applications, which is then negotiated contextually and situationally in the circumstances that arise for a given application before the committee. This moral intuition, built up from a lifetime of cultural experience, manifests in an ethics assessment undergirded as much by reason as it is by feeling, as one member explained:

> I think in ethics committees, as in life, we make very quick decisions, 'Oh, that's right', or 'That's wrong', and most of the time we're okay. And if there's very little contention, if there are no particular problems, it's a very efficient way to make decisions. (P10)

This is not to say RECs and individual members were incapable of justifying their reasoning; rather, it is that the moral reasoning could manifest *ex post* rather than a priori, or as one REC Chair put it: 'The actual ethical review process is almost tick-box' (P3).

Part of this can be explained both by the growth in volume of procedural forms provided by the HRA to REC members, and by the lack many REC members have in formal ethics education and training. REC members receive basic induction in research ethics issues and are encouraged to engage in self-directed learning,[21] but no member I spoke with thought such training would transform them into ethicists. Indeed, few members were interested in academic ethics articles or abstract ethical debates. In this sense, pragmatism drives the decision-making process: members apply rules, standards, and principles in ways that are practically useful for rendering a decision and that work best for the situation at hand. As one HRA regulator told me, 'there's a disconnect

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[19] Mary Warnock, 'Moral Thinking and Government Policy: The Warnock Committee on Human Embryology' (1985) 63 The Milbank Memorial Fund Quarterly: Health and Society 504, 518.

[20] ibid 520.

[21] Health Research Authority, 'REC Member Learning Resources' <www.hra.nhs.uk/planning-and-improving-research/learning/rec-member-learning-resources/> accessed 22 October 2019.

between where ethics is going as an academic discipline and where it talks about research ethics, and the knowledge of RECs about that and that sort of coming together to discuss, so that one informs the other' (P1). This seems to bother neither the HRA nor RECs—nor, from what I saw in my observations, researchers and sponsors. The important point that regulators and REC members equally stressed is that a REC must be able to justify an outcome that is reasonable: provided so, it will be seen as valid, legitimate, and ethical. As a REC Chair elaborated:

> I can't tell you how [as a REC member] to think, and that actually what I want to try and do is to get people to think: 'How am I deciding? What are the reasons for my decision? How am I reflecting on this? Where can I turn? What questions should I ask myself?' I think if one can provide that sort of framework, then it has to be down to the individual to look back to see, 'What are my own values?' When you come to an ethics committee, when you come to induction training at say whatever age you are, 30, 40, 50, 60, there's so much in your life that you bring to that, that this meeting for one day is going to barely touch. So I try to help people and say: 'Look, if you're going to make decisions, just work out what your reasons are because those are the crucial … Why have you made that decision?' By and large, if people think about reasons and think through their reasons, I think they usually come to the right decision. (P10)

As I continued to peer into these black boxes, I also discovered that in bringing their life experiences to bear in the ethics review process, REC members engaged in rituals that helped coordinate relationships, overcome potential disagreement, and achieve a consensus opinion.

2.1.2.3 Rituals in ethics review Ritual patterns are often present in highly 'rationalized' settings such as hospitals, and are embedded to a significant degree in the schedules, procedures, and practices of the setting.[22] RECs and the spaces in which they meet and constitute form a highly rationalized setting. In creating and reinforcing their ethics of space, REC members adopt rituals—that is, a type of patterned or institutionalized symbolic action[23]—that manifest throughout the process of ethics review. These include:

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[22] Nora Machado and Tom Burns, 'Complex Social Organization: Multiple Organizing Modes, Structural Incongruence, and Mechanisms of Integration' (1998) 76 Public Administration 355, 372.

[23] ibid.

- the refrain of phrases expressed by a REC Chair to the REC and attending researchers to induce comradery (a REC Chair might say to the attending researcher: 'Thanks very much for attending today. We've had a *really* good discussion of your application, and as you might expect, have a few questions for you'; following a face-to-face meeting with a researcher, a REC Chair might jokingly say to the researcher, 'Right, now run for the hills!'; or always begin the group deliberation following the face-to-face researcher meeting with, 'What do we think, team?');
- the ordering of questions gathered by the REC Chair (i.e. distilling the REC's discussion of an application into three or four key questions for the attending researchers so as to keep the meeting on time and also not overwhelm researchers);
- rituals of placement, such as the seating arrangement of REC members, researchers, and staff (e.g. the Chair and Manager always sitting side by side, researchers sitting at a right angle to the REC Chair and Manager, as opposed to directly across from them, which minimizes a sense of confrontation and encourages a more research 'promotionist' approach);
- the shuffling of the bundles of papers as RECs move through the applications, which perpetually swathe the conference tables during meetings;
- the presentation by the Lead and Second Reviewers to the REC by reading from their filled-in HRA Ethical Review Form;
- the meeting structure (e.g. on-time starts and a strong collective desire to stick to the allotted times for the agenda items); and
- the formalized structure of working through an application (i.e. the structure of Lead and Second Reviewer presentations followed by structured discussion by other REC members).

Rituals play a crucial role in structuring how members formulate comments on an application and approach their ethical decision-making. Similar group rituals were present across all five RECs, and within each, members had individual rituals vis-à-vis their review process. Thus, how rituals of ethics review played out varied across members. REC members bring their own idiosyncrasies and predilections to their reviews; they have 'certain bugbears' that can make them sound like 'a bit of a broken record' (P12), but this, members explained, helps ensure a well-rounded and consistent review. As a Scientific Officer told me: 'You also have to find your own way [as a REC member], because if everybody reviews an application the same way, you're going to miss something' (P23). Indeed, subjectivity and idiosyncrasy of individual members is a natural outcome

of most independent committee structures. The committee structure allows for a more thorough review than if only one reviewer is to pore over an application. Yet, it was rarely the case that subjectivity among individual members led to diametrically opposing viewpoints on the ethical acceptability of an application. Consensus forms the backbone of ethical deliberation, which is reached in large part through rituals:

> if there wasn't at least an element of opinion and subjectivity in the review process you wouldn't need committees. You could do the entire review with checkboxes on a computer. […] But I also think it's true to say that if you canvassed the committee members about what the decision for this month's applications would be before the meeting started, there would be almost complete unanimity on every application. (P14)

Some members review applications from only a narrow perspective, such as through their niche area of expertise (e.g. statistics, pharmacology). Others, particularly lay members, invoke a process of relationality: they read applications from the perspective of a potential participant, reminding themselves to 'think like a patient' and raise issues that may concern even only a few patients. In 'thinking like a patient', the lens may not be ethical per se; instead, it may be grounded in relationality with participants, tied in with an ethic of care:

> I take a step to the side and I think from the patients' or the participants' perspective; not that I sit and think I'm here because I'm a professional with a background in certain things. I would definitely highlight if I thought that the scientific integrity of a protocol wasn't robust, but really because I'm there as not a specialist or not an expert person. I give my opinion from the more personable side, patients' side. (P22)

Some members think it inappropriate, however, to substitute their opinion on whether to participate in a given project with that of an adequately informed potential participant. For these members, relationality with participants is risky; avoidance of paternalism should predominate. An ethical research project for them is one that discloses all material information to participants:

> I remember commenting on a particularly onerous … I think it was pancreatic cancer study. Even if I had the cancer and was as sick as I needed to be to enter the study, I personally would not be prepared to enrol in the study because of the demands it would place on me. It was too onerous. Having said that, was it ethical? Yes, absolutely, because you're telling the patients precisely what's going to be required of them. And whilst I wouldn't agree to it, that doesn't mean to say that other people can't. And that's actually

> potentially a difficult distinction to make. […] It was an interesting one for me because I wouldn't volunteer for the study, but I wouldn't say it's wrong for other people to do it. (P14)

As noted, one of the key rituals is the meeting and agenda structure for RECs. Established by the HRA in a template form, the meeting agenda was consistent across all five RECs I observed, namely in the order of:

1. Apologies for Absence;
2. Minutes of the Meeting Last Held;
3. Matters Arising;
4. Items for Information and Discussion;
5. REC Manager's Report;
6. Declarations of Interest;
7. New Applications for Ethical Review (led by the Lead Reviewer and then Second Reviewer);
8. Any Other Business; and
9. Date of Next Meeting.

Within this structure, the timing was constant, too. Items 1–6 rarely extended beyond five minutes discussion in total. The vast majority of each meeting was dedicated to Item 7: New Applications for Ethical Review. Following the presentation by the Lead Reviewer (which typically ranged from 7 to 15 minutes), the Second Reviewer added a few comments (typically ranging from 3 to 7 minutes) in a gap-filling manner, raising further queries to be posed to the researcher or areas of concern within an application. Then, the REC Chair would invite other REC members to comment on the application. Following this open discussion, the REC Chair would write down the 'main issues' to discuss with the researcher, assuming the researcher was attending in person. (REC Managers were always taking minutes of the meetings, portions of which would then be transformed into opinion letters sent to the researchers.) Once the list of questions was formulated to all members' satisfaction, the REC Chair or Manager would retrieve the researchers (along with, on occasion, a representative from the sponsor or a student's supervisor) waiting outside (assuming they were attending in person), invite them inside, and ask questions regarding the application. Following this back-and-forth dialogue, the researcher would leave, and the REC Chair would invite members to deliberate further on the application, culminating in a decision.

Rituals of expertise manifested themselves often in meetings. For REC members with a particular niche area of expertise, such as statistics, quite

often the REC Chair would turn to a specific member and ask, 'Are the statistics okay?' The member would reply, and then the REC Chair would move on. The power of the member's expertise was such that other members did not feel able to adequately comment on the specific matter of concern, though often other REC members would ask general questions about a niche area to the expert member, such as a pharmacist, prefacing their question with self-effacing and self-professed ignorance of the area.

Routine in the ethics reviews undertaken by individual members and routine in the meetings themselves do not necessarily mean there is a predictable outcome in any given application, even though the vast majority of applications (71 per cent from the meetings I observed) are deemed 'provisional'.[24] Interestingly, a provisional opinion is a *forward-focused* step in ethics review. The application moves from the pre-review threshold at submission to the threshold of approval during the REC meeting. A provisional opinion rendered by a REC almost always leads to a favourable opinion once the researcher has addressed the REC's concerns, which are expressed in the opinion letter. Indeed, members in all five RECs I observed sometimes would use the phrase 'provisional favourable' in announcing their verdict on an application, which symbolically differs from the HRA's term of 'provisional opinion', which signals no pre-determined final outcome. Upon receiving a provisional opinion, a researcher likely will amend the relevant documentation, which is then reviewed by the REC Chair and sometimes one or two other members, and then this 'sub-committee' will render a final decision.

With an array of rituals, idiosyncrasies, and moral intuitions, even if ethics is 'situated'—constrained by the limits of the committee structure, the predominance of scientific experts, or the desire for consensus and efficiency—any given REC's output, as with the input, is uncertain. For example, certain cues in the course of ethics review (e.g. the type of research under review, a REC's trust in the researcher, the quality—such

[24] Out of the 24 REC meetings I attended, I observed deliberation of a total of 119 new applications for ethics review. Six were approved outright as favourable, 22 were granted favourable with conditions, 85 were deemed provisional, and 6 were rejected as unfavourable. This is on par with the HRA statistics for RECs in England, which indicate that, of applications reviewed at full committee meetings, on average over 70 per cent are deemed provisional. See Health Research Authority, 'Annual Report Summary for RECs in England April 2016 to March 2017' <www.hra.nhs.uk/documents/1515/Annual_Report_Summary_for_RECs_in_England_April_2016_-_March_2017.pdf> accessed 22 October 2019.

as lack of errors and comprehensiveness—of the IRAS form and attendant documents) can help make an outcome more predictable, but not necessarily certain. There is always an element of uncertainty in the outcome of an application after REC review. As well, intra-REC precedent (i.e. comparing current applications to past applications and decisions) occasionally was invoked in deliberations to serve as a reference and maintain consistency, but this was not done formally or systematically. Instead, group experience, or a 'memory within the group' (P19), predominated the aiding of a decision. As one REC Chair phrased it, 'group moral maxims that we all generally share' (P10) helped determine if the past opinions were relevant to the current application. Collective memory and experience, along with these 'group moral maxims', maintained order and propelled the REC towards a decision that they believed would be consistent within their REC and, ideally, across others.

Liminality draws our attention to rituals and how they play a crucial role in regulatory coordination. The rituals in ethics review serve to organize the REC's actions, reinforce their authority, but also drive collaboration and coordination with other actors, particularly researchers. Rituals constitute embedded processes of ethics review that work to create shared meanings, establish order, build feelings of community, and encourage trust in the process and outcome. At the same time, in considering the ways in which research may be regulated by a network of regulators (e.g. RECs, MHRA, HRA) through a variety of rituals (e.g. rituals of consent, rituals of placement at meetings, rituals of words and phrases), we see that rituals have a tangible impact on the regulatory actors' behaviour, particularly when those rituals are disrupted by regulatory changes, or impositions 'from above', such as the HRA's ShED exercise or push for Proportionate Review. Liminality invites us to identify and pay attention to symbolically and practically significant rituals and how they organize a REC's regulatory behaviour and structure a REC's relations with other actors.

2.1.2.4 Ethics as an act of faith As a final key finding discovered when peering inside the 'black boxes' of RECs, ethics review can be an act of faith shared between the REC and researchers. This finding aligns with the sociologist Adam Hedgecoe's observation that RECs and researchers can interact as 'work groups' and co-construct 'organizational deviance' through 'cultures of production' that contain various features, including trust that RECs place in research applicants' abilities and

openness.[25] REC members receive 'marvellous bits of paper' in research applications, some of which may be 'meaningless' (P12), and yet they must make a definitive judgement on what they see and hear. For applications from commercial sponsors especially, REC members feel they must act on faith to trust the researcher or research team to act ethically. For them, there is a risk—but an acceptable one—in approving an application based on their assessment of 'bits of paper' and perhaps a 15-minute discussion with the Chief Investigator or another member of the research team.

A vital component that makes this act of faith acceptable to the REC, researchers, the HRA, and others is the face-to-face meeting with the researcher. This meeting follows the presentation of the application by the Lead and Second Reviewers and the general discussions around the conference table. REC members place a tremendous degree of value on meeting the researcher (or research team) in person, and likewise, though I did not interview them, researchers seemed to value the face-to-face meetings as well.

There are two purposes behind asking a researcher to attend a REC meeting. The first is to discuss key issues in the application that may be resolved in the meeting, thus saving time and perhaps even turning an application from a provisional to a favourable opinion. Efficiency and research promotion drive this purpose. As one REC member told me, 'because we can ask them questions straightaway and sometimes they can give answers very quickly, it just resolves the problem in a way' (P20). The second purpose is to get a sense of whether researchers seem trustworthy—something that cannot be investigated nearly as thoroughly through a document review alone. RECs want to get a sense of the researcher's character and probity. A good presentation by a researcher is almost as valuable as a well-put-together application. If the REC is comfortable that a Chief Investigator has participants' welfare at heart—and some members believe this is 'easy to convey in an interpersonal interaction' (P14)—then it will go a long way towards delivering a favourable opinion. Given that a number of researchers choose to apply to the same REC, either because the REC is in their local area or because they think highly of the particular committee, the rapport and trust established between REC and researcher can lead to more efficient—but potentially also shortcutted—reviews:

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[25] Adam Hedgecoe, 'A Deviation from Standard Design? Clinical Trials, Research Ethics Committees, and the Regulatory Co-Construction of Organizational Deviance' (2014) 44 Social Studies of Science 59.

> So [this researcher had] done all that she'd needed to do to use [the medical device]; she just hadn't explained it particularly well in the IRAS [form]. And she put us completely at ease [in the face-to-face meeting] that the safety wasn't going to be an issue. So along comes the second application [from the same researcher a couple months later]. It has essentially the same defect in terms of explaining the safety. But because we knew it was her, we knew it wasn't an issue and we didn't need to spend any time on it, because it was the same piece of kit. The same researcher, and she'd convinced us beforehand. So that was very helpful. (P14)

At the same time, the inability for the REC to observe the researcher in action, to monitor what is actually occurring, given its *ex ante* positioning in the research lifecycle, troubles some members. Even if they have a good 'feeling' based on the face-to-face meeting, how sure can they be that the researcher will conduct the project ethically? Again, faith must be placed in the researcher to act ethically: 'All we're approving is the paperwork in effect, and we have no control about what actually goes on' (P8). To sustain this faith, RECs must work together with other actors to share responsibilities, approve projects that are designed to be ethical throughout, and inculcate virtuous behaviour in researchers. And, in working with other actors, RECs must connect across regulatory spaces. I now unpack this as the second theme.

2.2 Regulatory Connectivity

Law and science occupy an uncertain relationship with the work that RECs do. The GAfREC indicate that RECs are not responsible for assessing the scientific quality and legality of a research project; after all, RECs are neither a scientific review nor legal advisory body. In regard to science, the GAfREC state that: 'A REC need not reconsider the quality of the science, as this is the responsibility of the sponsor and will have been subject to review by one or more experts in the field (known as "peer review").'[26] In regard to law, the GAfREC state: 'It is not the role of the REC to offer a legal opinion on research proposals, but it may advise the researcher, sponsor or host organisation whenever it considers that legal advice might be helpful to them.'[27] In regard to regulatory responsibilities (e.g. those undertaken by the MHRA or HTA), the GAfREC encourages RECs to defer to other bodies where responsibilities may overlap: 'Where others have a regulatory responsibility, a REC can expect to rely on them to fulfil it. If the law gives another body

[26] GAfREC para 5.4.2(a).
[27] ibid para 3.2.11.

duties that are normally responsibilities of a REC according to this document, RECs do not duplicate them.'[28]

Even if RECs 'need not reconsider' scientific quality, should not offer a 'legal opinion' on research proposals, and should not 'duplicate' other bodies that have regulatory responsibilities, it remains the case that often they perform all three roles.

2.2.1 Ethics and science

REC members find it a 'constant struggle to try and separate out the idea' that RECs already should be assured that the science is 'good' and that the application has had appropriate peer review (P1). As a body partially comprised of past or current researchers, it is a challenge for many to disentangle science and ethics, as even HRA regulators recognize:

> you have a certain number of experts 'round there who are all jobbing scientists and jobbing researchers, or much of them are, or at least acquainted with research at that level, you know, who can't help but pick over the carcass and the bones of the methodology … It's really difficult … where does ethics stop? Where do you stop thinking it's an ethics issue? But I think they do predominantly, a lot of committees do focus on the methodology, talk about the methodology. (P1)

Indeed, the HRA seems to implicitly acknowledge this potential for a connected ethics-science regulatory space in its push for committees to include a statistician among their membership. The GAfREC state that: 'The REC will be satisfied with credible assurances that the research has an identified sponsor and that it takes account of appropriate scientific peer review.'[29] But how does a REC satisfy itself with such credible assurances? A good deal of discretion is given to them. Not surprisingly, even REC members who are not 'jobbing scientists' also think it vital to ensure the science 'is right'. Three different members I interviewed repeated a well-worn line in research ethics: Bad Science is Bad Ethics. But they also acknowledged that RECs cannot simply mimic scientific review committees. In consequence, RECs engage in a secondary form of *self-policed* science review.

There were times that I observed RECs expressing uncertainty with the scope of their scientific review, particularly in their communications with researchers. For example, when a statistician expressed serious concern

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[28] ibid para 5.4.2(c).
[29] ibid para 5.4.2(a).

about the stated scientific accuracy of a CTIMP application, the Vice Chair remarked, 'this is a MHRA issue, though'. The statistician countered that the MHRA advises on research design, but not accuracy. Self-policing itself, the REC as a whole discussed how best to express this to the applicants, deciding that they could *not* say in the opinion letter that they disagreed with the scientific design, but instead they would ask the researchers to more clearly explain their rationale for the project design, given 'concerns' the REC had. In other instances where I observed that RECs felt the science of a proposed research project was not up to par, they policed themselves in terms of not having it colour their overall assessment of the application; their concerns would be expressed in the opinion letter, but the opinion was to be based on a constricted view of the 'ethics'. There was an ongoing challenge, therefore, in teasing out the ethics from the science. Invariably, the resulting opinion was not a favourable one—not surprising in itself when only six applications were granted 'favourable' outright, which equates to 5 per cent of the total new applications I observed.[30] The evidence suggests that RECs constrain themselves within their own linguistic and operational paradigm or 'space', implicitly recognizing there is another regulatory space (i.e. science review) that they ought not to enter explicitly. Through these constraints or workarounds, RECs can satisfy themselves that the ethics of an application has been fully reviewed to their satisfaction, and in a way that does not penetrate too deeply or too explicitly the scientific space.

Is this an instance of 'double jeopardy'?[31] I do not believe so. The ethics-science divide is an artificial boundary incapable of being rationally adhered to in this process of review.[32] RECs do not seek to expand their jurisdictional control over science. If anything, REC members admitted hesitancy in assessing scientific quality, but the process of ethics

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[30] This practice endorses David Hunter's argument that bad science is poor ethics, but not necessarily bad ethics, and thus not grounds for rejection alone. See David Hunter, 'Bad Science Equals Poor not Necessarily Bad Ethics' in Jennifer Gunning and Søren Holm (eds), *Ethics, Law and Society: Volume III* (Ashgate Publishing 2007).

[31] Stephen Humphreys and others, 'Science Review in Research Ethics Committees: Double Jeopardy?' (2015) 10 Research Ethics 227.

[32] See also Angus Dawson and Steve Yentis, 'Contesting the Science/Ethics Distinction in the Review of Clinical Research' (2007) 33 Journal of Medical Ethics 165 (arguing that the science versus ethics distinction is incoherent and that RECs have an 'obligation' to consider a research project's science).

review necessarily entails a verification of the scientific quality.[33] The CIOMS Guidelines endorse this position in their latest version, which states: 'Although in some instances scientific review precedes ethical review, research ethics committees must always have the opportunity to combine scientific and ethical review in order to ensure the social value of the research.'[34] My empirical findings also accord with those of other researchers who found that scientific issues (e.g. sampling; choice of methods; the research question; the measuring instrument; analysis; bias; feasibility; equipoise) are frequently raised in opinion letters to researchers and are often considered a quality problem by RECs.[35] One REC Chair explained the connectivity thusly:

> [An application] might have the best question in the world, it might have the best hypothesis, but if the way the research is designed has not been able to answer that question, then there is a danger that time, effort, and money are all going to be wasted. Participants' time could be wasted and for me that is unethical and shouldn't be allowed to happen. (P3)

RECs want to be satisfied the science is sound, so unverified reliance on the scientific review alone will not suffice.[36] To the extent there is a 'problem' of regulatory overlap, it is not one of double jeopardy, but rather one of a science paradigm that is prevalent within RECs (unsurprising when we consider that so many members are current or former medics or scientists) and of a failure in regulatory frameworks to

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[33] This runs against the logic circulating in the EU Clinical Trials Regulation No 536/2014, which separates ethics review from the review of the science. Controversially, the latter review explicitly includes assessment of the risk-benefit ratio. Unsurprisingly, the Regulation has been criticized for the effect it will have on REC operations and the adequate protection of research participants. See e.g. Eugenijus Gefenas and others, 'Application Challenges of the New EU Clinical Trials Regulation' (2017) 73 European Journal of Clinical Pharmacology 795; Carlo Petrini, 'What is the Role of Ethics Committees after Regulation (EU) 536/2014?' (2016) 42 Journal of Medical Ethics 186.

[34] Council for International Organizations of Medical Sciences, *International Ethical Guidelines for Health-Related Research Involving Humans* (Council for International Organizations of Medical Sciences 2016), Guideline 23, Commentary.

[35] Emma Angell and others, 'An Analysis of Decision Letters by Research Ethics Committees: The Ethics/Scientific Quality Boundary Examined' (2008) 17 BMJ Quality & Safety 131.

[36] See also Sarah Edwards, 'The Role, Remit and Function of the Research Ethics Committee—2. Science and Society: The Scope of Ethics Review' (2010) 6 Research Ethics Review 58.

acknowledge the *necessary* overlap in review as between ethics and science. If RECs are constituted to review, among other things, risk to participants, they necessarily must have due regard to the scientific design that generates such risk, and not merely regard to the value of the science alone.

Previewing discussion to come on regulatory stewardship, some REC members suggested that they could focus less on the science in their reviews if there were better support for a research design service at the nascent stage when researchers and sponsors are planning their projects. Stewards such as the four Scientific Officers in the Scottish RES, though highly qualified and experienced in both science and ethics reviews, cannot perform this role alone:

> It's great having Scientific Officers, but it's, like, how far can we go into the science of the application? And there isn't an obvious other person to send [researchers] to, you know, 'cause you're thinking, oh I should … the science of this … this hasn't been designed very well, this study. … they're overlapping, aren't they, science and the ethics. But you, kind of, feel that you can only go so far down a certain line. So it is a great service up here, but, you know … there's always something missing, isn't there. (P27)

2.2.2 Ethics and law

Similarly, many REC members thought it necessary to have due regard for relevant laws. An ethics opinion is not a legal opinion, but it is certainly informed by the law. Moreover, for some RECs, such as the Scotland A REC, they *must* have due regard for legislation in their functions.[37] Statutory regulations now ascribe specific functions to ethics committees (e.g. the Clinical Trials Regulations 2004, Mental Capacity Act 2005). REC members are aware of the importance of law in undertaking their reviews, as a REC Chair told me:

> When I joined my committee back in 2003 … when I first applied, I was turned down, and the reason I was turned down was because one of the questions I was asked was whether the ethics committee should consider the law or not. And my response was, 'Yes, we should consider the law.' And that was the reason I was turned down. It was the wrong answer! At the time, the

[37] For the Scotland A REC, this includes the AWI Act and the Adults with Incapacity (Ethics Committee) (Scotland) Regulations 2002/190, as amended. Notably, again evidencing the regulatory connection between ethics and science, Regulation 6 of the Regulations makes clear that the Scotland A REC 'must take into account' in its review 'the objectives, design, methodology, statistical considerations and organisation of the research'.

> view was ethics committees consider ethics and the law to lawyers. Nowadays, that would be the right answer. You cannot undertake an ethical review without considering the law, and very many bits of it. But whether we reference it an awful lot, I don't think we do. Other than the Data Protection Act … (P3)

Yet unlike scientific quality, which most REC members feel is important to consider and discuss regularly, as the REC Chair above indicated, rarely did I observe RECs explicitly considering the law when discussing an application at a meeting, and members did not suggest to me that they consulted the law when conducting an ethics review remotely prior to the meeting. Rather, I observed that RECs encouraged researchers to see it as their (and their sponsor's) responsibility to assure compliance with the law, both when designing their project and when conducting the research. REC members agreed that their opinion is not a 'legal opinion', but they strive to ensure their opinion is *intra vires*—that is, to provide an ethics opinion that sits within the bounds of legality. Most REC members interviewed did not feel a lawyer was needed on a committee. As a member of NREAP told me:

> the ethics committee is not making a legal judgement—what they're doing is providing advice that's consistent with the legal framework that they're having to operate within. That's how I see it. Now, is that operating according to a legal framework or not? I think it is. And it's daft to say the law doesn't have a grip on ethics committees. It does. But it's not on everything. Again, you might say, well practice is around consent, or data management, being engaged with the common law as well as statute. I don't think you can escape from it, but you don't have to be a lawyer to be on an ethics committee. (P4)

The HRA does provide training on relevant areas of the law, such as patient confidentiality; data protection; research involving children; the Mental Capacity Act 2005; and the Human Tissue Act 2004. For REC members, that was seen as sufficient. After all, they are charged with only having 'regard to statutory provisions for ethical review of particular types of research'.[38] Much of the assurances about legality provided previously from the R&D (i.e. research governance) directorate or R&D offices in England are now from the HRA Approval team, known as 'HRA Assessors', who conduct the review remotely. REC members do not want to render an opinion that is blatantly illegal, but they also do not want to carry the weight of expectations that their opinion is as much legal as it is ethical. As with science, the ethics opinion necessarily

[38] GAfREC para 3.2.10.

incorporates consideration of the law. The regulatory spaces are connected, but not necessarily combined. As one member of the Scotland A REC told me, again emphasizing the liberal approach:

> I think there is a bit of a tension between training people in, say, the Data Protection Act, that you are sort of handing them a mantle, in a sense, and empowering them to believe they understand the law and, therefore, are making legal decisions around data protection. I think that's a mistake. […] [I]t ought to be around the sort of ethical issues involved in handling data and whether it's appropriate, and whether it's clear and open, and people understand what the deal is and it's a fair choice that's being offered. (P12)

This liberal approach manifests itself most clearly when RECs confront grey areas of the law. RECs must make a good judgement that is consistent with the law, even if they may be unsure of whether their opinion is suitably legal. For example, when a REC reviews an application where adults with incapacity might be enrolled in a project, a specific checklist is consulted so that members ensure that all relevant elements of the Mental Capacity Act 2005 or Adults with Incapacity (Scotland) Act 2000 (AWI Act) (whichever applies) are observed. The HRA assures RECs the checklist is not meant to be seen as rigid; rather, it serves as an aide-memoire, for the Lead Reviewer in particular, to consider when reviewing an application.

Other times, RECs are genuinely uncertain of the legal effects of a research project. One REC in England I observed, for instance, was uncertain whether researchers looking to start a UK-wide research database legally required a separate REC approval in Scotland. In another REC meeting I observed, a REC member queried other members what would happen if participants lost capacity during a Phase 1b CTIMP. The REC Chair recalled that, under the Medicines for Human Use (Clinical Trials) Regulations 2004, if a patient has capacity to consent at the beginning of the trial, that consent continues through for the duration of the trial, unlike for research projects subject to the Mental Capacity Act 2005. But he also expressed some doubt. He then looked at me and said, 'Edward?' I pointed to my 'Observer' name plate, reminded the REC of my duty to not speak during the meeting, and everyone laughed. 'Oh, twist his arm!' the Chair joked. 'Okay, I'll look this up and get back to everyone on what the rules are,' he added.

Members of the Scotland A REC have particular expertise with the AWI Act, and those who have served for a long time on the committee are critical of the Act's provisions relating to research. Indeed, this REC's special focus on the AWI Act seemingly enables them to be more flexible in their interpretation of the law than other RECs I observed,

who are mindful in obeying and strictly interpreting the research-related provisions of legislation such as the Human Tissue Act 2004 (only one section of which applies in Scotland). The AWI Act's provisions state that research involving an incapacitated adult is forbidden unless: (1) research of a similar nature cannot be carried out on an adult who is capable in relation to such a decision; and (2) the purpose of the research is to obtain knowledge of the causes, diagnosis, treatment, or care of the adult's incapacity; or the effect of any treatment or care given during the adult's incapacity which relates to that incapacity. One of the conditions of such research is that consent *must* be obtained from any guardian or welfare attorney who has power to consent to the adult's participation in research or, where there is no such guardian or welfare attorney, from the adult's nearest relative.[39] What does this mean for research projects on emergency treatment? A strict interpretation would suggest that it can hardly ever be performed. However, Scotland A REC members found that both ethics and law have shades of grey in interpretation, and part of their role is to craft an ethics opinion that respects the spirit of the law without taking a necessarily conservative view:

> People often say, well, of course, ethics is very grey, but the law is very black and white. And you go, well, no, actually it really isn't. And I think there is … yeah, and I think that's the problem actually with the AWI thing and this absolute requirement for consent. It's never been tested in court, got no idea if there is actually an absolute requirement. No one has ever challenged it and said, well, hang on a minute, I wouldn't normally ask people [for consent] who are capable. There is no other way of doing it, this is a really important question, it's an emergency situation, for example. It's just a complete nonsense. I think you could well find that actually a judge might say, yeah, you're right, it's complete nonsense and start to refine it, but there's never been that. So there's this belief that it's against the law but actually as you know, laws don't really work like that. (P12)

In sum, the connections between ethics, law, and science cross-cut across regulatory spaces. RECs and other actors such as the HRA Assessors who assess governance and legal compliance as part of HRA Approval can receive the same pile (or digital file) of documentation but approach them with differing goals and perspectives. A REC strives to focus its assessment on ethical issues, but inevitably there is some duplication in the process, as RECs and other bodies move across fluid spaces of ethics, law, and science. The research application and its attendant documents

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[39] Adults with Incapacity (Scotland) Act 2000, s 51.

involve a network of regulatory actors and resources embedded in several interconnected and overlapping spaces. These documents form a dynamic nexus or focal point that circulates throughout the network. The HRA wants its guidance for REC members on relevant legislation (e.g. Mental Capacity Act 2005) to be reflected in the REC opinion letters, but this appears to be more for quality control check purposes. Adding reference to the law changes the force of an ethics opinion letter. As one REC Manager (P15) told me, 'they're not just ordinary letters that we do. I think of them as legal documents.' If a researcher appeals a REC decision, the HRA and another REC can always look at the initial REC and trace what has happened, including whether there was inappropriate information or opinion given about relevant legislation. In this sense, then, a REC must not only always be aware of the legal implications, but also strive to provide adequate assurance that a participant's legal rights are being protected and due process is followed.[40] This is a shared task; other actors involved in health research regulation also must play a part in reaching an outcome that is ethical, scientifically robust, and legal. Thus, despite what the GAfREC state, and despite what some critics label a fundamental problem, RECs do engage in scientific and, to a lesser degree, legal review. This is seen as a responsibility that may be shared with, but not delegated to, other bodies.

To conclude this theme, RECs are embedded in multiple overlapping, interconnecting regulatory spaces. The REC floats within and between these spaces. The evidence suggests that in regard to science and the law, the REC space is the connecting bridge between these other spaces. In this sense, the REC is truly liminal. Rather than viewing these overlapping regulatory spaces as a problem, we would be better served to view them as evidence that regulators can act as stewards—that is, they can help researchers and others navigate the various spaces.

2.3 Relationships, Protection and Promotion, and Stewardship

A final theme to emerge from the empirical investigation concerns the nature of the interactions between RECs and the HRA, the variation in mechanisms to work through the ostensibly twin roles of participant protection and research promotion, and the value of regulatory stewardship in guiding researchers across the stages of the research lifecycle. The research findings reinforce Árpád Szakolczai's contention that in

[40] Christopher Roy-Toole, 'Research Ethics Committees and the Legality of the Protocol: A Rejoinder and a Challenge to the Department of Health' (2009) 5 Research Ethics Review 33.

liminal moments, there is often an independent actor serving as a 'master of ceremonies' to guide people (and things) through rituals, moments, or periods of transition.[41] It is here where I wish to bridge to Chapter 6 in drawing out implications for health research regulation as it concerns embedding 'processual regulation' and regulatory stewardship more visibly into regulatory frameworks.

2.3.1 Interests and responsibilities

REC members view themselves relationally, as key nodes in a network of regulatory spaces that, together with other actors, perform tasks that aim to mediate between science and society and between the spaces themselves. Vis-à-vis researchers, REC members found that only in rare instances would researchers fail to appreciate the value of an ethics review, dismissing it as a bureaucratic step that they should not have to face.[42] Quite often, REC members reported that researchers view RECs as a helpful body that can improve their research and ensure risks towards participants are minimized. In turn, REC members viewed their committees as stewards that can encourage researchers and support them in conducting robust and ethical research.

Members expressed that the interests of RECs, researchers, and the HRA are aligned, and the common bond is in facilitating meaningful research. We should recall that a good number of REC members are or have been researchers themselves; they do not sit in a silo, viewing research from only one side. As a REC Chair explained it, 'it's all tied up' (P3), and as another Chair added, REC members, researchers, and other stakeholders form a common community: 'I don't see it as two different communities. I see it as one community trying to learn together. We all have common aims—researchers, research ethics committees, the public—and that's relevant, meaningful, and valid research. And promoting that I think is a shared task' (P10). Linking this to the above discussion about scientific quality and the discussion to follow about research promotion, RECs are confident in suggesting changes to applications to support researchers, not just in terms of ethics, but also in

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[41] Árpád Szakolczai, 'Liminality and Experience: Structuring Transitory Situations and Transformative Events' in Agnes Horvath and others (eds), *Breaking Boundaries: Varieties of Liminality* (Berghahn 2015).

[42] REC members tended to dismiss these researchers as 'older researchers who don't fill in our IRAS application forms, don't know how to, because they get their juniors to do it'. They were viewed as unchangeable; RECs simply must wait 'until they retire' (P23).

terms of scientific quality. This is something that the HRA recognizes and encourages:

> [REC members are] strongly encouraging in terms of what different parts of the application could be changed or how things could be done slightly better. They're just good at giving advice to researchers. Often, we receive feedback from the researchers saying it was really helpful to attend the meeting and encouraging. And one thing—we have used the satisfaction reports and we added a question to it to say, 'Do you think the REC review enhanced your study?' And we felt that that was quite a brave question for us to put on. We weren't sure what sort of feedback we'd get, but I think about 75 per cent are saying, yes, they do feel the REC review enhanced their study. So that's been really good to see as well. (P26)

While the relationship between RECs and researchers may be seen as healthily aligned, as already noted above, the relationship between RECs and the HRA is more complicated. As we saw from Chapter 3, for years, RECs, and especially LRECs, operated as local fiefdoms. The move towards centralization with COREC and NRES caused entrenched positions to be taken. One regulator told me that a running joke among RECs was that every time NRES put out guidance to RECs, it was dismissed as yet 'another missive from central bunker' (P1).

None of the members I interviewed took such a negative view of the HRA, but their assessments were certainly mixed. A REC Chair described the relationship today as 'collaborative' and 'a team effort' (P3) with regard to sharing aims. A few other REC members I spoke with were generally supportive of the HRA, finding there is a 'reasonably open channel' (P7) of communication with them. However, others I spoke with felt that they were 'completely unaware of what goes on at the HRA' and that constant regulatory changes served as a distraction. A REC member expressed her frustration to me as such: 'Who do they [the HRA] think they're collaborative with? To me, they send an email to the REC Managers and then the REC Managers forward that on. That's as collaborative as it gets.' She explained that she and other members adopt a cynical approach to dealing with the HRA:

> So, I think at the last meeting that you were at, somebody said, 'What's this for, what's HRA Approval mean?' […] And honestly, as a REC member, we don't really get told anything in a way that is digestible, understandable. And, to be honest, it wouldn't actually change how we reviewed the documentation anyway. A study is a study regardless. With my researcher's hat on, my real-world job, we have to be very aware of what's going on, and, to be honest, it's not communicated brilliantly. Because all my colleagues, our mantra is don't bother to learn the system because the next time you come to

> put in an application it will be completely different. So, let's go with the flow. If we do it wrong, they'll tell us. (P8)

Similarly, members offered mixed assessments about the ShED exercise and Proportionate Review. Focusing on the former, members felt that ShED provides the HRA with some idea of whether and where RECs are broadly consistent or inconsistent. One member described it as 'very helpful' for training purposes and improving 'everybody's education' in terms of what to 'look for' in an application (P7). Similarly, an HRA regulator explained that they find ShED adds a lot of value in highlighting where the differences are across RECs and how they can 'be addressed through further training' (P17). The same REC member who adopts a cynical approach to dealing with the HRA, however, described ShED as 'absolute dross':

> Oh God, when we used to get them at [XXX] we used to go, 'Oh, not another one, what is the point?' So we'd do it, and I will tell you this, I always realized that I was always leading on it, and then the REC Manager admitted to me, 'Oh yes, because I know it will get done properly […], we need to make sure it's done properly so we look good.' Okay. Honestly, everybody's heart sank every time we got one. So you'd review it, and you would do it properly, and then several months later you'd get this consolidated report of, well, so many committees said this and so many committees said that. … And the point of that is? So, what is the actual answer? […] What is that actually teaching us? I've no idea. […] … utter nonsense. There must be a better way of doing it. I mean, it's to ensure consistency. […] Maybe it's useful for them because they can tick a box. That's me being cynical again. But I can't say I've ever learned anything from doing it. (P8)

A Scientific Officer told me that the HRA acknowledged members are 'quite unenthusiastic about' the exercise (P26) and were working to improve the individual feedback to RECs. The HRA was of the view that individual feedback would provide RECs with an 'incentive to review [the ShED application] well and show how good they are, in a way' (P26). Yet even with these improvements, in discussions with members, scepticism seemed to predominate. Two members told me the last time their REC received a ShED application, they were assigned as Lead and Second Reviewers. Yet they were not told it was a ShED application, much to their frustration, and so they 'wasted three hours on it', complete with typed up notes. 'ShED is about the principles, not the practice. And they never told us! Needless to say, the HRA got some choice words from us,' one of the members told me. Laughingly, he then added that their REC had not received another ShED application since.

I also observed ongoing frustration with the HRA when a ShED application appeared before one of the RECs. The Lead Reviewer began her presentation by stating, 'I've put at the top of my paper, "Many queries".' The members laughed and nodded in agreement. The Lead Reviewer then added that she only realized *after the fact* that it was not a real application. Reading from her typed up HRA Ethical Review Form, which included sections highlighted in yellow that warranted particular discussion, she read out a litany of problems. 'Well done so far!' the REC Manager said as she was copying down each 'problem' noted by the Lead Reviewer. 'Are there any other ones?' she asked. 'As if that wasn't enough?' a member retorted. Nevertheless, other members then chipped in to add several more concerns. It became quickly evident to me that as part of this 'game', the more 'ethical problems' spotted by a REC, the more favourably the HRA would view them. A long-standing member, visibly frustrated, stated that previous ShED exercises had 'somewhat normal applications. But I gave up halfway through this one because I found it an insult, with a bunch of doctored information.' Other members verbally voiced their agreement. In response, the REC Manager explained the background to this particular ShED application. A private clinical trials unit sent this 'case' to the HRA's Director of Operations with a list of all the issues to spot. The REC Manager, sympathizing with the committee, added that she had already explained to the HRA her problems with this kind of 'spot the error' game, including how it is a poor use of the REC's meeting time. All REC members agreed with this assessment. The long-standing member added: 'I think the Shared thing is a good idea. But this …', she trailed off, waving her hand over the application. The consensus from the members was that the application contained too many small issues and not enough 'meaty ethical issues'. A member opined that a lot of the issues in the ShED application had been seen in real applications, but they were points more for researchers to pick up and learn from than for REC members. The discussion closed with the REC Manager asking the REC if there were 'main ethical issues to flag'. The REC members listed what they considered to be the main issues, with the REC Manager taking careful notes.

For some, then, the HRA was seen as an active central regulator that served the interests of the research community, but not always those of the REC community. Some REC Chairs were unclear who to contact when they had broad ethical questions or concerns. REC Managers and Regional Managers were seen as 'so overworked and busy just managing the day job of running committees' that they lacked 'any kind of mental space' (P11) for addressing broader concerns or issues. Members indicated that they would appreciate more interaction with the HRA to

understand the context of the next-generation regulations—but only to a certain degree. Just as they would appreciate more value for the work they do, members also wanted to retain their independence. A growth in procedural regulation and centralization caused some to worry that they were 'being told how to think' (P10); achieving a balance between quality ethics review (through consistency and standards set by managing regulators) and independent ethics review (freedom for an individual and a group to engage in ethics deliberation) was an ongoing struggle.

In sum, RECs viewed themselves as having aligned interests with other actors in regulatory spaces. Specifically, they perceived a close bond with researchers, sharing the same goal of facilitating meaningful and ethical research. RECs and the HRA also share this goal, but the relationship is more strained. The HRA was not always perceived as working collaboratively with RECs and at times was instead seen as interjecting itself into their ethics of space, causing tension and political controversy. What this suggests is that there is a plurality of regulatory spaces and a relationship between regulatory actors that constitutes a space at times filled with tension. But it also suggests that there are spaces between spaces. As we will see, there is a stewardship role *within* these spaces that appears to work well for Scotland and could work for other nations. If RECs perceive aligned interests, the question remains how they work to operationalize those interests. Specifically, how do they work through participant protection *and* research promotion?

2.3.2 Working through protection and promotion

I now return to one of the driving questions of this study—that of how RECs act among themselves and interact with other actors within the context of 'next-generation' regulation that aspires to both protect research participants from harm *and also* promote health research through streamlining perceived regulatory barriers. Going into the empirical research, I was expecting a number of REC members to express concern on two levels: first, that they had noticed a recent change in the regulatory architecture governing their practice as ethics reviewers; and second, that this change—an imposition of research promotion—was having detrimental effects on their ability to protect research participants.

As I discovered, REC members expressed a different viewpoint. For them, protection and promotion could be a challenge to work through (and at times was seen as being in 'tension'), but it was a twin role they recognized *and supported*. This twinned objective was therefore viewed not as a recent development or challenge in light of the Care Act 2014 or other statutory regulation, nor was it necessarily 'felt' by REC members. Rather, statutory regulation instantiating research promotion was seen as

a form of next-generation regulation that embedded in law what had been occurring in practice for a number of years. That it was now embedded in law did not translate into a shift in the relationship between RECs and the HRA, nor with researchers themselves. No member I spoke with was aware of explicit instructions issued by the HRA or other managing regulators encouraging or mandating them to look towards facilitating research while protecting participants. There was no explicit change in approach, and none felt that protection had been or was being sacrificed on the altar of a research promotionist agenda. To the contrary, some even thought RECs had become *more* protectionist in certain areas, such as no longer permitting researchers to look through patient notes without consent.

Many viewed research promotion as an example of their REC's independence and a key role for them to play, particularly for research that was independent (i.e. not funded by pharmaceutical companies) or may otherwise have been neglected (e.g. rare disease research). And, the aligned interests between RECs and researchers was such that the latter came to appreciate the assistance RECs provide in tweaking their application, be it on research design or a more standard 'ethical' component such as the consent process. The RECs I observed and members I spoke with wanted researchers to come to them with enquiries; they saw part of their role as being educational for researchers. They wanted researchers to regard ethics review as a favourable experience where RECs offer guidance and suggestions to improve their research project, foremost ethically but also scientifically. In this way, if researchers were to apply to the same REC, the REC would hope researchers take on board the issues they raised with them in a previous 'round' so that there would be a general improvement of standards.

This said, some recognized that the twinned protection and promotion role has become more pronounced compared to the previous generation of the ethics review system before COREC and subsequent efforts to centralize and standardize the RESs in the UK. If participant protection was the 'be-all and end-all' of RECs in the prior generation, next-generation regulation encourages all to view research as a civic good that requires promotion; part of the HRA's role is to 'help facilitate the set-up' of research (P2) and provide confidence to the public that good research is being conducted. Research promotion is intertwined with a bioeconomic imaginary that sees the UK as a favourable jurisdiction in

which to conduct research and bring economic benefit to the country.[43] As an HRA regulator explained:

> I think there's been a wholesale change if we just focus, say, on ethics committees, a change of emphasis … Before when I joined 20 years ago, running ethics committees, it was all about protection of the individual participant and that was pretty much it. That was the be-all and end-all, that's what we were there to do, protecting the individual participant. […] I think over time that's changed, that now we see research as a kind of civic good, something that people should have access to. You know, we need to break down barriers so that everyone can get access to research, so I think there's a shift between being protected from research and now being given access to it because it's a good thing. Also, our dual mission now is this sort of protection of the individual but facilitating ethical research and the whole making the UK a good place to do research, so that it comes in a UK PLC business kind of focus to what we're doing, that it's not about just protecting individuals, it's about making sure that the UK attracts research and money, and so that's the change, and people will have their views about that. I remain neutral on that. […] I think I just observe that that's been that shift, that things have become, well, commoditized, I suppose, in a way that research is part of UK PLC, attracting research here, doing research, making research easier, less bureaucratic, everything else, is all good for the, as I say, UK PLC. So there's been a shift there, I think, for ethics committees. Now whether that has been reflected in the people who sit on ethics committees … (P1)

RECs, however, were not consciously aware of any political pressure to realize this bioeconomic imaginary. They were cognizant of drivers that exert a strong influence on research promotion through streamlining initiatives, such as HRA Approval, the IRAS application, and changes in regulations that build the UK's research capacity and seek to harness patient records from the NHS. But they viewed their role, and the HRA's role in this drive, as but a 'small piece of a much larger jigsaw' (P5). Their independence is well preserved; they did not fear a present or future context in which they were pressured to 'skim' through application materials. 'I'll be honest with you,' a Scottish REC member confided in me, 'sometimes I think the UK wants to be seen as a biomedical hub and it is becoming a biomedical hub and it's good that it becomes [one], but it should never be at the expense of ethics and of protecting patients, never' (P20). This member was adamant that RECs would not allow this to happen.

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[43] Rustam Al-Shahi Salman and others, 'Increasing Value and Reducing Waste in Biomedical Research Regulation and Management' (2014) 383 Lancet 176.

If the HRA regulator I interviewed above was uncertain whether REC members embodied this dual mission of protection and promotion, accepting that it was indeed present in REC practice, there was also widespread variation regarding how this dual mission was to be worked through. As I came to discover, in the absence of specific guidance on how to work through protection and promotion, members approached this twin role through various heuristics. The HRA regulator speculated that protection and promotion is an *irreconcilable tension*, or as one REC member labelled it, 'an inherent contradiction' (P14), which simply must be acknowledged:

> I think we just acknowledge that tension [between protection and promotion]. Well, some people say there's no tension, other people say that's clearly a tension between those two things and you can't do both and there's a conflict of interest in doing both. I would love to tell you there was some practical way in which we sort of tell people how you balance that … like this is how you balance these two competing … but in practice, there is no guidance. We don't have a position on how you do that, we just hold these truths to be self-evident. You've got to protect but also you have to promote. (P1)

Yet later, when I pushed for clarification on how the HRA expects to foster an environment of protection and promotion if they do not offer practical guidance for RECs on how to work through this dual role, several interviewees came to view protection and promotion not as twin aims to be balanced, but rather, as aims to be treated *sequentially*, working from protection as a primary question that establishes a track record of trust, and only after to address a secondary question of research promotion:

> I suppose it's resolved by you treat[ing] them sequentially. The first one is you have to make sure that it's safe, risk-free and protected, and ethical, and if it is, well, you do everything you can to promote and facilitate that. So maybe it's resolved by that sort of sequential looking at it. You're not holding them at the same time, you're focusing first of all on the protection. Once you're assured of that protection, then we need to make sure that we don't then hang around on giving a decision for six months or something, that our processes are … that we can give that full due consideration to the protection in the time that we need to do that, but also make sure we deliver those opinions sort of rapidly so that that facilitates the research and it can go ahead. (P1)

> the protection is almost you have to get in the right order. We can't promote until we have something to promote and in order to promote it we need to make sure that everything is safe, is protected, because otherwise there's no point promoting something that no one has any trust in. […] In order to build

> up trust you need a track record. You can't just say, trust us, we're the NHS. It doesn't work. People don't work like that. I would say track record is more important. (P2)

Some REC members reiterated to me that 'participant safety and the ethics are always going to come first', as one put it:

> Standing back and looking in, definitely it's most important to promote research. Absolutely. But as a REC member, when that 12-inch thick pile of paperwork lands on my desk, my job is, as I see it, to read and evaluate those documents to make sure that those studies are scientifically sound or ethically sound and, on balance, no harm is being done to any participant. That's the bottom line. Whatever goes on from a management, HRA point of view, at that point I don't actually care. I care about that cancer patient or that healthy volunteer, that's what's important and that's what I'm assessing, as I see it, for me. (P8)

On the ground, facing research applications, other REC members saw protection and promotion *as working together*, as 'all tied up in one' (P3), with RECs and researchers both aiming for high-quality research. But how exactly do they work together? RECs will not often 'stop research from happening' (P3). The vast majority of research still goes ahead; indeed, the RECs I observed were extremely hesitant in rendering an unfavourable opinion and spent a significant amount of meeting time trying to work an application with a number of issues or concerns into a provisional opinion. When in the few instances I observed that a REC did render an unfavourable opinion, they aimed to phrase the opinion letter in a positive light, 'welcoming a resubmission' to the REC provided the researchers took their (suggested) points into account.

Some see the 'proportionate' approach taken by RECs to research applications as a mechanism to instantiate research promotion. By treating a 'simpler' project with a lighter touch than a more 'complex' or 'risky' project—typically seen as Phase 1 CTIMPs—RECs are contributing to the research enterprise. Others see protection as being '*balanced*' against promotion—or as one described it, as a 'halfway house' (P14)—with promotion as a value that can reign in a tendency to go overboard with protection:

> The idea that RECs are there to support ethical research for the common good, I think, is an appealing principle. It's one that I certainly support. But it's also one in which you're trying to balance the interests of the vulnerabilities of participants, the resources in health care and those kinds of thing. RECs definitely do feel very much, and they ought to, as they're there to offer a layer of protection for participants. But they can overstep the mark on that

> I think, and sometimes become too protectionist, or make some kind of claim about their own expertise, which oversteps what they can do. (P4)

Both a REC Chair in England and a Scientific Officer in Scotland opined that balance manifests in weighing the rights of the community against the rights of the individual, a balance that is difficult to achieve but fundamental to modern research. The primary interests will always be participants, but in contrast to the Declaration of Helsinki's Paragraph 8 precautionary intonation that medical research can *never* take precedence over the rights and interests of individual research participants, sometimes, the REC Chair told me, we must 'recognize that there's more than one person at this party and that we have to accommodate their interests' (P10); RECs must support research for the benefit of the community. Humorously, he added that RECs should promote research as a civic good to the community, to 'educate them and say, actually, research is a good thing for you. Research, like Guinness, is good for you' (P10).

Research that was poorly designed disappointed REC members, not so much because it was seen as a waste of their time, but because the underlying research question could be valuable and could 'save some lives'. A delayed research project was a delay to potentially innovative medical treatments and health care improvements. 'We want to find a way; we always want to find a way,' the Chair of one REC said as they were agonizing over the potentially too burdensome consent process for patients in an emergency setting. 'I love the idea of this proposal,' a Secondary Reviewer of a CTIMP said at one meeting, who went on to express concerns about how the researchers planned to execute it (specifically, the changing of dosages). 'It's such a shame,' he lamented. 'The study needs to be done, but perhaps in a different way.' Others agreed. 'I think it should be done, but they've got to get the application right.' In this instance, following a face-to-face interaction with the research team, the REC reached consensus on a provisional opinion, in which they would reiterate their concerns and hope to prod the research team to consequently redesign part of the CTIMP.

Whether through 'balance', 'ranking' or 'proportionality', RECs strive to work through protection and promotion, performing a twinned task that aligns their interests with that of their managing regulators, researchers, participants, and the public at large. The ways in which RECs help researchers navigate through thorny regulatory and ethically challenging areas can vary. In Chapter 6, I argue that this is in fact a *benefit* of next-generation regulation. Law, especially through the Care Act 2014, has provided sanctioned spaces in which RECs and other actors can engage in 'regulatory play', with more flexibility to work through

challenges and interact with others. Before I turn to this argument, however, in the final part of this theme, I further suggest that actors within and connected to RECs serve as 'stewards' who help guide researchers (as well as sponsors), and their protocols, across stages of the research lifecycle.

2.3.3 Regulatory stewardship

Regulatory stewardship can be defined as the prudent guidance of one or more actors across regulatory thresholds—without which there is risk of failure, impairment, or harm—with a view to fulfilment of regulatory objectives and collective betterment.[44] In this book, I have already ascribed importance to specific actors within regulatory spaces, and specifically those actors connected with RECs. Regulatory stewardship draws attention to more than just the REC; it highlights the role actors within or connected to them play in helping researchers, sponsors, REC members themselves, and others navigate difficult regulatory spaces and improve the overall quality of the research enterprise. In addition to the HRA, certain REC actors, namely REC Chairs, REC Managers, and Scientific Officers (as well as the REC as a unitary actor), play a critical role in assisting researchers and sponsors navigate the demands of putting an application together and channelling it through the various thresholds in the research lifecycle. These actors can serve as regulatory stewards that help researchers cross thresholds, serving as 'ethical research promoters'.

How does regulatory stewardship manifest in the operations of regulatory actors? An HRA regulator provided me with early insight in describing that Authority's vision for improving regulatory pathways, in part by providing support and working in partnership with other actors:

> ethics committees 90-something per cent of the time say yes to research, so actually [REC approval is] an arbitrary milestone and actually it's unhelpful because people are running towards it, putting in poor quality [research], which means that further downstream there are blockages. So, what we want to do is try and allow there to be [fewer] blockages downstream by improving the quality upstream and by providing support upstream, and along the way we should be able to help with that.
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> […]

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[44] Adapted from Graeme Laurie and others, 'Charting Regulatory Stewardship in Health Research: Making the Invisible Visible?' (2018) 27 Cambridge Quarterly of Healthcare Ethics 333.

> Medical research is hard. We see 6000 applications a year for medical research; it is hard, and we need to be helping these people realize their ideas rather than just being what's seen as a bureaucratic block at the beginning of something that is a very long process. Also, I guess there's the obligation there again not to waste money by blocking things, not to stop things because they are illegal. Obviously, we can't let them go through, but it's providing the support to enable people to realize their goals on an ongoing basis. But again, I think it's working in partnership with other people. (P2)

The HRA's role as a regulatory steward is manifest at varying levels. At a high level, there is guidance on the HRA website for researchers, in terms of best practices, policies, and regulations. HRA interlocutors told me they aimed to provide researchers and sponsors with as much information as they could upfront so that when an application came to the REC, it was as good as it could be at that point in time. At a more granular level, the HRA in the past has, on an interim basis, created 'Application Managers', who helped researchers navigate through complex cases that straddled regulatory regimes, such as those involving multiple domains (e.g. data, tissue, and devices), and piloted an 'Ethics Officer' role, which will be discussed briefly below. In Chapter 6, I argue that in embedding regulatory stewardship into the regulatory framework, there is room for the HRA to further improve their practices.

Regulatory stewardship also is manifest in the REC itself. REC members, individually and as a group, saw themselves as providing a kind of upstream pastoral support to researchers. They serve to protect the rights, interests, and welfare of research participants, but equally, they felt as though they serve to promote ethical research by *working with* researchers. RECs are removed from the 'real happening' of research, but in any event, their role is not to monitor the day-to-day practice of research. There is a distinction to make here between a steward and a gatekeeper. A gatekeeper monitors and may also enforce and sanction. A steward, however, helps others navigate difficult terrain and inculcates values and principles that are embodied and instantiated in everyday practices. A REC's role is to evaluate the ethical acceptability of a research project and to help researchers (and to some degree, sponsors) navigate complex regulatory terrain, insofar as that regulation is of an ethical nature, though we have seen that this necessarily overlaps with science and law. It is also a REC's role to encourage researchers to comply with approprate regulatory and professional standards in the way they conduct themselves as researchers. Researchers are in a position to inform RECs of the latest trends and issues in research, as well as to report back to them their experiences in working through ethics reviews

and other regulatory processes. Viewed together, this dynamic is mutually reinforcing.

To be clear, the stewardship practised by REC members is not necessarily direct and deliberate (and indeed RECs cannot write an application or protocol for a researcher), but through nudges, comments, and responses to queries, members help assuage or even persuade research applicants to improve the quality of their research design or work around a false roadblock in law (e.g. a misinterpretation that data protection law or adults with incapacity law is stricter than it really is regarding research). Even though a few REC members and Managers were hesitant to view RECs as promoting research or serving as advisers to researchers ('we're not there to spoon-feed the researchers on how to do their job', one Manager told me), in practice, across all five RECs I observed instances of a stewardship function at every meeting. From this I gathered that for some members, research promotion is an unconscious role that is wrapped up in the process of their review. Ethics review is not a static event of compliance with a checklist of standards (though three members complained that it can feel as such with the HRA Ethical Review Form). Instead, it is a dynamic process whereby researchers, the application, and protocol are carried across thresholds by various actors, including the REC, who suggest 'better ways' to devise a project and thereby shepherd it forward.

A few examples from my observations illustrate this finding. Scotland A REC members reminded researchers that if they asked participants for consent to follow-up their medical records, it would allow them five years of follow-up without any additional cost. Not infrequently, other RECs offered suggestions to improve recruitment numbers for a project, pleasantly surprising the attending researchers. 'Not a question, but a suggestion,' a statistician remarked to one group of researchers. 'Speak with a local statistician and mention "case control" to them. What you're doing isn't wrong, but you may be able to get more out of what you're doing.' During a face-to-face encounter with a researcher proposing a substantial amendment to a genetic research project, the researcher explained that her original protocol and PIS stated that all data related to the participant would be destroyed if the participant chose to withdraw. A REC member intervened at this point and encouraged the researcher to think about modifying the documents, should she want to retain the data collected and analyse the data up to the point of participant withdrawal. The researcher, unaware of this possibility, thanked the REC member for this suggestion, but then wondered whether this approach would properly constitute withdrawal and would respect the participants. The REC Chair

replied that 'there's no clear answer' but thought withdrawal would be unlikely anyway. He encouraged the researcher to 'think about it'.

Face-to-face interactions with researchers also illustrate this stewardship role. A Scotland A REC member relayed a story about the fluid ontological boundary between 'research' and 'audit' in contrast to its strict regulatory boundary:

> We had one very interesting study from [England] that was […] wanting to study care homes, and it was just going to be … it was a sociological study, and of course in the care homes were the people with incapacity. And we advised them that in Scotland, if they did this as an audit of what was going on in care homes, it would be very appropriate to go ahead. If they did it as research, then they couldn't look at patients in the care home who had … lacked capacity, because what they were trying to study had nothing to do with their disease. It took about four letters to the committee, to the researchers. So, we gave them a solution. All they insisted on saying was, yes, they agree, we'll do this as an audit on one care home in Scotland, but because in their perception it had to be seen as being research, to get the funding or to get validated or whatever it was down south, they didn't grasp that we were trying to open up the way to let them do it, it wasn't actually going to involve any interventions in patients that were in the care home. But they just couldn't actually do it without getting consent from everyone if they did it as a research study. (P18)

REC members were encouraging of regulatory stewardship at different levels, from the more complex cases involving interpretations of law, to simpler instances of ensuring an IRAS application is correctly filled in. One member considered it useful to 'triage' the application before it came to the REC (perhaps in coordination with sponsors, R&D offices, or others), looking at mundane issues such as grammar but also regulatory and ethical issues. This suggests a need for stewardship at an earlier stage of research design and approval and, indeed, throughout the research lifecycle. Better triaged applications would lead to higher quality, more error-free applications at REC meetings, allowing RECs to focus their time on substantive issues. Instances of why this would be useful were observed in REC meetings. During one, the REC Manager explained to the REC that the researcher ticked a certain box in the IRAS project filter, which opens up certain questions for the IRAS ethics application form. Had the researcher clicked 'basic science' instead, it would have been much clearer for everyone when it came to performing the ethics review. The REC Manager further explained the application was transferred from one HRA Regional Office to another, which caused it to fall through the cracks. Neither a REC Manager nor HRA Regional Manager went back to the researcher to support her before she submitted

the application, and the application was accepted in the early round of the validation process. 'It has snuck through validation, unfortunately,' the REC Chair sighed.

Though the REC itself can serve as steward, regulatory stewardship is evidenced most clearly in the work of actors in greater positions of authority or influence within a committee, namely Scientific Officers and the REC Chair and Manager, all of whom have closer contact with researchers. Between the monthly full committee meetings, REC Chairs receive a volume of correspondence from researchers asking for advice. REC Chairs told me they were happy to provide support because 'it helps to create the right environment' and achieves the shared end goal of 'high quality good research that's going to make a difference to people's lives' (P3). Through this support service, REC Chairs saw themselves as 'promoting research. I think the committee, as the committee's representative, I am promoting research in the UK and encouraging it, and trying to get it started as quickly as possible' (P3). Similarly, REC Managers saw their role as stewarding researchers through the application process:

> I'm here to try and help the researcher really to make sure that their information gets put across as well as possible. […] Part of my role is almost trying to pre-empt the questions that the committee will be raising as well. So, something obvious that's missing and I know the committee will look for, I can ask the researcher beforehand and that's to try and facilitate to try and get the application through for them as smoothly as possible. (P25)

Throughout my year-long observations and interviews, the four Scientific Officers in Scotland's RES were universally praised for their role in providing educational and regulatory support to RECs, researchers, and sponsors alike.[45] The CSO created the position in 2008 in response to the 2004 Lord Warner Report's recommendation.[46] Appointing one Scientific Officer in each of Scotland's four main regions was seen as a way to: (1) have Scottish RECs conform to national standards across Scotland, rather than local Health Board standards; (2) allow for Scottish RECs to better link with the CSO to ensure best practices were disseminated and ensure RECs were using the same documentation, databases, rules, and guidelines; and (3) help researchers get their applications through more

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[45] Indeed, one Scientific Officer (P23) told me that it is not unusual for researchers in England who are submitting applications to an English REC to contact a Scientific Officer for advice.

[46] See Chapter 3 for discussion of the Lord Warner Report.

efficiently and make Scotland an attractive destination within the UK to conduct research.

Scientific Officers sit side by side with REC Managers on a daily basis, which, unlike in England, allows for constant interaction and more efficient communication with researchers and sponsors. Their side-by-side interaction with RECs also helps prevent RECs from getting bogged down in unnecessary details, as one Scientific Officer explained to me:

> we [Scientific Officers] are appreciated by the committees—that we can kind of just protect them from just getting bogged down with too many queries and things. Where we absolutely come into our own is all the queries at the pre-application stage are completely directed towards us and nothing goes through to the committee members or Chairs at that stage. And I think that makes a big difference. (P24)

Scientific Officers provide researchers and sponsors with guidance and support on a variety of matters, including compliance with correct documentation and conformity with legal requirements, all of which could impact the success of their research application and their research as a whole. At the same time, Scientific Officers help guide REC members in evaluating research applications, particularly when it comes to understanding the regulatory context of a given application:

> the other part was making clear that the committees are not just there to be a gatekeeper, but they're also there to try and facilitate research. So we should be talking to … the Scientific Officers should be talking to researchers about how to do research, especially to sponsors about what the committee expects to see, and also to the members to explain that if you get a difficult application or an application that mentions previous ones, we should be helping the committee understand what's going on with applications, and keeping committees, committee members up to date with training. (P16)

Scientific Officers not only help researchers with the ethics component of their application; they can also help guide them to other regulatory steps needed for approval:

> The other thing is to remind [researchers] that ethics isn't the be-all and end-all. You're going to need R&D approval; that's going to take roughly this amount of time. And part of our job, which I might come back to, is because we have interactions with those people, we give researchers some guidance. […] If I give advice to somebody, they might say, it's nothing to do with ethics. And so, I'm not doing this from an ethics point of view, I'm doing this as it facilitates research point of view, because I know that R&D will ask for this. […] [Researchers] forget that part of [our] job is a facilitatory role and

> it's not just … it's not trying to catch people out who are doing the wrong things. (P16)

A Scientific Officer (P24) explained that if RECs see a local university consistently submitting applications that 'aren't up to scratch for different reasons', then they look to identify what the specific problem areas are and work with the university to remedy them for improved future applications. Another Scientific Officer (P27) distinguished the REC's task of ethics *review* (which, in her mind, is focused more on compliance with standards) from the 'office' in which she sat, which focuses more on science and serves as an ethics *advice service*, with researchers viewed as 'clients':

> There's the committee and there's the office. And I think in the office we perceive the applicant, as it were, like our clients. So, you do all that you can to help them get through the process so that you're not blocking that application. So, we're quite … we're trying to be very friendly and, you know, trying to tell them the information that they need to give us. But sometimes it is a bit like Chinese … you know … well not quite Chinese whispers, but, you know, you're trying to help them through the process, so we have that strong feeling. (P27)

England has not gone the route of Scientific Officers, but the HRA has been equally keen to support researchers. Unlike Scotland, however, embedding regulatory stewardship within a specific actor equivalent to a Scientific Officer has presented challenges. As explained to me by an HRA regulator, the HRA conducted an 'Ethics Officer' pilot in 2012 as a potential avenue for supporting researchers through the application stage by providing them with advice on preparing for attendance at the REC meeting following submission of their application. According to the regulator, it was not a success. REC Chairs, who took the lead as Ethics Officers, attended *other* REC meetings as supporters of researchers. REC members apparently felt uneasy or even threatened by having an 'outsider' REC Chair attend their meeting and comment on an application, which they felt was their responsibility (and considering the above discussion about black boxes between RECs and an ethics of space, we come to understand why). More recently, the HRA contemplated rolling out a 'REC Application Review and Advice Service' that encouraged REC Managers to conduct an 'enhanced check' on an application submitted to their REC. This would have involved looking at the project-specific documents and thinking about potential administrative issues that needed fixing. One HRA regulator explained that an example would be if a REC Manager

> knew that their committee were likely to ask for a certain aspect of the information sheet to be changed, […] they would pick that up with the applicant and say you're likely to be asked to change this, you can either change it now before the meeting, but you may still be asked to make extra changes after the meeting depending on what the committee say in their review. (P26)

Of course, this role differs from what Scientific Officers do, as the latter also provide help on matters of scientific design and legal interpretation. A further twist is that with the introduction of HRA Approval in England, HRA Assessors are picking up administrative discrepancies and inconsistencies as well. If, for example, the protocol said one thing but it was described differently in the PIS, both HRA Assessors and REC Managers would be picking this up. Due to the duplication 'between the two teams' (P26) and the concern that it could cause more confusion for applicants in terms of being contacted by two different people for two sets of issues, the HRA has scaled back on REC Managers conducting enhanced checks, such that this is only now done for Phase 1 CTIMPS with healthy volunteers, which are not eligible for HRA Approval and thus not looked at by an HRA Assessor. Regardless, my impression of HRA Approval is that it is more of a 'compliance check' process than an opportunity for stewardship whereby actors within the HRA not only remove barriers, but also help facilitate better research. Stewardship, to the extent it operates currently within the HRA, will be found in other processes carried out by other actors.

To this end, the HRA now encourages: (1) researchers to consult the HRA's online decisional 'toolkits'; (2) researchers to email queries to HRA staff; and (3) REC Managers to look carefully at the research applications before the REC meetings and 'think about what ethical guidance they might want to point their committees in the direction of' before the meeting (P26). The HRA also wants to 'empower' REC Managers to think about what laws and ethical guidance the REC might want to take into consideration when reviewing applications so that the discussion is 'focused more on the ethical issues' (P26), and so that in the opinion letters, there is more explicit reference to guidance to explain the REC's reasons for why they are requesting changes to the application or rendering a provisional or unfavourable opinion.

Whether this is a role that REC Managers can successfully take on, given their competing demands, remains to be seen. The Scientific Officers I spoke with contrasted their roles with REC Managers on numerous grounds, including the educational differences between them. Scientific Officers have tended to hold PhDs in a scientific field; REC

Managers may or may not hold university undergraduate degrees. Because of this, REC Managers may be unable to read an application as expertly to understand the ethical, scientific, and legal issues at play. Regardless of these challenges in England, the HRA is committed to providing a robust ethics guidance and support service to researchers. As I will argue in the next chapter, however, more can be done to embed regulatory stewardship in the health research regulatory framework, and the HRA is positioned to take a leading role here.

III. CONCLUSION

Informed by anthropology of regulation methodology, this chapter examined the ways in which practices, people, and entities are structured in and by health research regulation, and vice versa. The findings reveal a critical understanding of REC practices and the form and function of health research regulation. The findings also reveal a processual and experiential understanding of RECs and the ways in which they affect and are affected by regulation.

The data suggest that modifications to the health research regulatory space at the levels of statutory law and central regulatory authorities have not so much 'trickled down' to the day-to-day practices of RECs, as the day-to-day practices have long reflected what has only recently been enacted in law. RECs, the HRA, and researchers share a common goal of promoting research that is safe and of high quality. They carry similar interests and shared responsibilities, helping each other to cross boundaries and deal with major moments of transition in the research lifecycle. However, a concern that emerges from the research, and which I address in Chapter 6, is that the respective roles, competencies, and influences among the actors are not always clear, and the regulatory conversations are sporadic and at times weak between regulators (the HRA and RECs), though relatively strong between regulators (RECs) and regulatees (researchers). Consequently, spaces can appear *within* the health research regulatory space where hazards may occur.

In the next chapter, I suggest a normative model of what a new regulatory framework, informed by these empirical findings, ought to look like. The empirical data suggest that the REC's stewardship role has the potential to reach *beyond* the *ex ante* stage of research, that is, before the research project begins. The hybrid protectionist-promotionist model that operates in practice fosters an environment that both protects research participants *and also facilitates* responsible health research in the country through proportionate regulation and coordinated alignment

of ethics review and other regulatory processes. This can be operationalized not only at the initial stage(s) of the research lifecycle, at the moment of research design and initial application, but also, I will argue, throughout the lifecycle—importantly in partnership with other regulatory actors—where ongoing opportunities for 'regulatory play' can emerge.

Thus, in Chapter 6, I argue that, in the absence of an expressed theory of how the objectives of research promotion and participant protection should be achieved, a theory (or decision framework) should be crafted that may not invariably hinge on the mechanism of balance. If we envision RECs as evaluating research projects in stages and acting as gatekeepers and stewards at several thresholds, how can health research regulation, including at the level of legal architecture, take up the insights from liminality to provide a suitable space to capture these stages of dual commitment and realms of possibility? How might a regulatory framework, which legally must be 'proportionate',[47] enable regulatory stewards to take charge in accommodating potential harms and maximizing research outcomes? And how can law help create a space within which there is more room to protect and promote, a space for more epistemic latitude—a realm of possibility—for RECs to 'roam in' and experiment together with other actors, including those who may have cross-cutting motives? We now turn to see how the empirical findings from an anthropology of regulation may help build such a regulatory framework for stewardship to flourish.

[47] Care Act 2014, s 111(3) and Department for Business, Innovation and Skills, *Regulators' Code* (UK Government 2014).