

Chapter 6

Responsible research and
innovation

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The concept of ‘responsible research and innovation’ (RRI) has been adopted by policy-makers as a way of thinking more systematically about the public benefits of science and technology-based research. The precise definitions and constituent elements of RRI remain matters of debate and can appear abstract, so here we suggest six priorities that apply specifically to RRI in the context of novel neurotechnologies.

- **Clearly identified need:** It is important to justify innovation in terms of its public benefits. In the case of neurotechnologies this means meeting therapeutic need. This highlights the need to resist the technological imperative and the pursuit of novelty for its own sake. It also challenges the value of proliferating products that are indistinguishable in terms of the benefits they bring to patients.
- **Securing safety and efficacy:** Protecting safety is central the pursuit of RRI and to regulatory regimes governing medical technologies. Where the clinical uses of novel neurotechnologies are concerned, their risks can only adequately be assessed relative to their efficacy in delivering therapeutic benefits and the (possibly limited) availability of alternative treatments. This highlights the importance of assessing efficacy as part of the innovation pathway of a product – yet this is not a regulatory requirement for medical devices (such as those used in TBS and DBS) marketed in Europe.
- **Generating robust evidence:** There are both regulatory and methodological reasons why the development of medical devices in particular might not produce the most transparent, robust or balanced body of evidence. These include un-generalisable and dispersed data from small-scale studies, the influence of commercial interests, and methods that encourage the publication of positive, but not disappointing, findings. Alternative methods of linking and disseminating evidence are likely to be needed to address this.
- **Continuous reflexive evaluation:** The development of novel neurotechnologies is unlikely to follow simple linear innovation trajectories. Reflecting upon the directions in which research is (potentially) travelling, and responding to this, can help to guard innovation against lock-in to pathways that do not serve public benefit. It is also an important part of maintaining vigilance for implications of possible unintended dual-use or ‘off-label’ applications of neurotechnologies.
- **Coordinated interdisciplinary action:** Innovation in novel neurodevices, perhaps most markedly BCIs, is often multidisciplinary. Coordination between different disciplines is needed to protect against potential risks posed by gaps in the collective understanding and oversight of a technology’s risks and capabilities. Interdisciplinary collaboration also offers opportunities by introducing diverse visions of potentially fruitful development trajectories.
- **Effective and proportionate oversight:** The tension between need and uncertainty that lies at the foundation of our ethical framework presents a particular challenge to effective regulation and governance of novel neurotechnologies. Responsibility and humility require caution whilst also recognising that failing to pursue interventions also carries risks of extending suffering in the absence of effective treatment. This demands a proportionate approach to supporting innovation while protecting safety; hard-law regulation will not always be the most suitable means of achieving this.

This articulation of RRI provides a tool, complementing our ethical framework, which we go on to use to assess the strengths and weaknesses of the regulatory frameworks that govern the commercial availability of novel neurotechnologies. The concept of RRI also acts as an extension of our virtue-guided approach by highlighting the ways in which inventiveness, humility and responsibility should inform the practices and values of those engaged in supporting and pursuing innovation.

Introduction

- 6.1 In this chapter and the next we apply our ethical framework to the challenges generated by the *development* of novel neurotechnologies themselves. On the basis of this framework we may understand that the central goal of innovation in this field is to deliver therapeutic technologies to those who need them. This is tempered by caution to avoid harm to these individuals and to avoid intervening in the brain unnecessarily, or where evidence of efficacy or unanticipated consequences remain unclear. The various actors involved in the development of these technologies must exercise the virtue of responsibility by striking a balance between these twin imperatives. Here we chiefly focus on the activities of those directly engaged in funding, conducting, and steering research and innovation endeavours. However, it is not possible to draw a definitive line around this class of actors. For example, as Chapter 5 makes plain, much exploration of therapeutic applications of these technologies will take place in experimental treatment contexts, making many clinicians ‘developers’ too.

6.2 The approach we appeal to in this chapter is based around the concept of ‘Responsible research and innovation’ (RRI). There is increasing support amongst policy makers for a systematic approach to RRI as a practical lens through which states and actors are encouraged to think about technology development. It has notably been adopted as a key cross-cutting theme under the prospective EU Framework for Research and Innovation “Horizon 2020”.⁵⁹⁹ The critical discourse surrounding the aims and component aspects of RRI is still evolving and subject to debate.⁶⁰⁰ For this reason, component elements of various RRI frameworks vary. They nevertheless share a common emphasis upon the achievement of public benefits through science and technology-based research. This entails securing ethically sound and scientifically robust research objectives, conduct, and governance.⁶⁰¹ RRI can be viewed as being as much about fostering practices and cultures amongst those engaged in supporting and pursuing innovation as a concern with appropriate regulatory and governance structures. The engagement of publics in determining what the desirable ends of research are, and how innovation processes can achieve these, is also often seen as a crucial part of responsible practice.⁶⁰²

RRI in the context of novel neurotechnologies

6.3 In Chapter 3, we highlighted how funding gaps in the development trajectories of neurotechnologies from laboratory to commercial product – and the resultant economic pressures upon developers – might drive innovation practices (particularly in relation to neurodevices) towards those that focus upon swift financial returns, potentially at the expense of meeting the public interest in safe, effective, and well-evidenced therapies. Attention to the demands of RRI can play an important role in characterising how developers’ intentions should be refocused. RRI should not, however, be understood as antithetical to profitable commercial activities. A recent report prepared for the European Commission emphasised that early consideration of an RRI approach in a field of innovation can help to ensure that research funding is not wasted and to identify developing fruitful markets that meet social needs.⁶⁰³

6.4 The concept of RRI, as often construed, remains rather generic, pegged at a level of abstraction that permits them to be applied across different contexts and different technologies. Our purpose in this chapter is to establish what this concept looks like in the context of the novel neurotechnologies with which we are concerned, to make it more concrete and thus of practical use both to those conducting and funding research and to those involved in governing this field by guiding the discharge of their responsibilities. In the context of this report, understanding what is entailed by RRI can, alongside our ethical framework, provide us with the tools to assess the strengths and weaknesses of existing approaches to regulating the development of neurotechnologies and their entry onto the market.

⁵⁹⁹ European Commission: Research and Innovation (2013) *Horizon 2020*, available at: http://ec.europa.eu/research/horizon2020/index_en.cfm?pg=home&video=none. See also: European Commission: DG Research and Innovation (2011) *A report on responsible research & innovation*, available at: http://ec.europa.eu/research/science-society/document_library/pdf_06/rri-report-hilary-sutcliffe_en.pdf.

⁶⁰⁰ European Commission: DG Research and Innovation (2011) *A report on responsible research & innovation*, available at: http://ec.europa.eu/research/science-society/document_library/pdf_06/rri-report-hilary-sutcliffe_en.pdf; Owen R, Macnaghten P and Stilgoe J (2012) Responsible research and innovation: from science in society to science for society, with society *Science and Public Policy* **39(6)**: 751-60.

⁶⁰¹ Von Schomberg R (2013) A vision of responsible innovation [forthcoming], in *Responsible Innovation*, Owen R, Heintz M, and Bressant J (Editors) (London: John Wiley).

⁶⁰² For example, Nuffield Council on Bioethics (2012) *Emerging biotechnologies: technology, choice and the public good*, available at: http://www.nuffieldbioethics.org/sites/default/files/Emerging_biotechnologies_full_report_web_0.pdf includes an in-depth discussion of how public discourse may shape normative propositions about the direction and governance of innovation.

⁶⁰³ European Commission (2013) *Options for strengthening responsible research and innovation*, available at: http://ec.europa.eu/research/science-society/document_library/pdf_06/options-for-strengthening_en.pdf.

6.5 We suggest the following six elements as priorities for the RRI of novel neurotechnologies. These are derived from the discussions of this report up to this point: the current state of the art of these technologies; the economic forces operating upon their development; and our ethical framework:

- Clearly identified need
- Securing safety and efficacy
- Generating robust evidence
- Continuous reflexive evaluation
- Coordinated interdisciplinary action
- Effective and proportionate oversight

Clearly identified need

6.6 Recent debates regarding synthetic biology have suggested that researchers in that field must be able to justify their endeavours in terms of what they hope to achieve and their beliefs about how they will get there. Those supporting research (for example through funding, institutional ethical approval, or policy) also need to look beyond technical excellence to ask what social good an emerging technology serves.⁶⁰⁴ These questions are equally relevant to the pursuit of innovation in novel neurotechnologies.

6.7 Unwarranted intervention in the human body is always hard to defend, but this is particularly true of the brain. Our ethical framework construes ‘need’ in this context in terms of a therapeutic priority to alleviate the suffering of those living with the effects of neurological or mental health disorders. Inventiveness is a virtue when directed at these ends, while remaining mindful of the enduring uncertainties of intervening. RRI of novel neurotechnologies entails being able to justify innovation in these terms.

6.8 Of course, this does not mean that the pursuit of foundational research, for which a need for particular translational applications cannot yet be clearly articulated, is excluded. However, the criterion of ‘clearly identified need’ provides a valuable benchmark against which to assess the relative merits, in terms of social value, of any predictable directions to which such research could be applied. This could be of use, for example, in weighing up the respective opportunity costs of pursuing divergent research questions or development pathways where resources such as professional expertise or facilities are limited. A precept that challenges developers and funders to attend to need warns both against pursuing the merely novel and the largely imitative. On one hand it questions the wisdom of following the technological imperative, where existing therapeutic interventions might be more effective or accessible. On the other hand, it highlights the lack of value in adding to a proliferation of similar technologies, distinguished only by superfluous or trivial modifications that serve manufacturers’ economic interests rather than patients’ needs.⁶⁰⁵

Securing safety and efficacy

6.9 RRI must deliver safe neurotechnologies as outputs – this much might seem self-evident. It is nonetheless important to draw attention to safety in order to be able to pose questions about what its significance is in practice.

6.10 Safety is one of the key considerations of the regulatory regimes governing whether neurodevices or neural stem cell therapies receive approval to be marketed in the UK and the rest of Europe. However, as we note in Chapter 3, regulatory routes are available that permit

⁶⁰⁴ Biotechnology and Biological Sciences Research Council (BBSRC) and the Engineering and Physical Sciences Research Council (EPSRC) (2010) *Synthetic biology dialogue*, available at: <http://www.bbsrc.ac.uk/web/FILES/Reviews/1006-synthetic-biology-dialogue.pdf>, pp. 7-9.

⁶⁰⁵ Von Schomberg R (2013) A vision of responsible innovation [forthcoming], in *Responsible Innovation*, Owen R, Heintz M, and Bressant J (Editors) (London: John Wiley), at page 5.

medical devices to receive marketing approval on the basis of safety and performance evidence relating to previously approved devices.⁶⁰⁶ These may be attractive to manufacturers by removing the delay and costs of the need to demonstrate safety through clinical studies. However, unless it can be adequately demonstrated that the device in question and that to which the existing evidence pertains are sufficiently similar in function and effect, exploiting these routes represents a failure in the protection of patients' interests and in transparency, which runs contrary to responsible innovation.

- 6.11 Moreover, considerations of safety must be assessed in relation to the degree of any likely benefit that can be expected and the nature of any foreseeable risks. This means that information about the *efficacy* of an intervention in delivering purported therapeutic benefits will be a crucial part of determining whether safety – once established below a certain threshold – is of an acceptable level. In meeting therapeutic need and protecting patients from unnecessary harm, it is therefore important that the oversight mechanisms determining the availability of these technologies look beyond safety as an isolated consideration. Where regulations governing neurotechnologies do not require demonstration of efficacy⁶⁰⁷ – as in the European regulation of neurodevices – this could be seen as an important gap in being able to understand safety in its proper context (see paragraph 7.17).

Generating robust evidence

- 6.12 The development of neurotechnologies must proceed on the *basis* of the best available evidence to minimise risks to research participants. Humility and responsibility counsel that, where there are evidence gaps, these must be acknowledged and accounted for throughout the development pathway. It is just as important that the processes of innovation also *generate* robust evidence; not least to satisfy the conditions of demonstrating the two conditions of RRI outlined in the preceding sections by demonstrating that neurotechnologies are effective, meet therapeutic needs and do so without posing disproportionate risks. The availability of such evidence is also essential to support autonomous decision-making by patients and research participants (and therefore their valid consent), and to ensure that interventions in the brain only occur when there are scientifically and methodologically sound grounds for doing so. The virtue of inventiveness drives this pursuit of knowledge, but must be matched by responsible practices with respect to conducting research and reporting findings.
- 6.13 There is a *prima facie* hurdle to gathering robust scientific evidence in the field of novel neurotechnologies. As we have already noted, the kinds of serious neurological and mental health disorders for which novel neurotechnologies are indicated will often mean that limited numbers of individuals are eligible to participate in large-scale research studies such as randomised controlled trials (RCTs) (see paragraph 5.55). We explore further in Chapter 7 why RCTs may not be best suited to the characteristics development pathways for medical devices in particular (see 7.37 to 7.38). Clinical investigations of neurotechnologies will therefore often proceed through small scale studies and experimental treatment rather than large clinical trials. However, a landscape of small dispersed investigations may not be best suited to gathering a consolidated body of knowledge upon which to assess the promises and risks of these technologies. Dispersed experimental findings, and indeed unanticipated adverse events, may not be published or widely disseminated, and even where they are, studies with small numbers of participants and varying protocols can generate un-generalisable data.
- 6.14 Further considerations arise from possible threats to research and publishing integrity that may result from the sheer novelty of these fields of research and the kind of hype that might be

⁶⁰⁶ European Commission (2009) *Clinical evaluation: a guide for manufacturers and notified bodies*, available at: http://ec.europa.eu/consumers/sectors/medical-devices/files/meddev/2_7_1rev_3_en.pdf; Cohen D and Billingsley M (2011) Europeans are left to their own devices *British Medical Journal* **342:d2748**: 1-7, at page 2.

⁶⁰⁷ Cohen D and Billingsley M (2011) Europeans are left to their own devices *British Medical Journal* **342:d2748**: 1-7, at page 2.

driven by competition for investment and funding that we have already discussed in Chapter 3. The need to attract funding perhaps inevitably leads to overstatement of the capacities and benefits of technologies under development. Commercial interests may further militate against transparency by seeking to treat studies as commercially confidential or by blurring the lines between impartial clinical investigation and sponsored use of medical devices by paid clinicians (see paragraphs 3.66 to 3.70). Particular methodological and reporting practices may contribute to this hype. For example, there is an acknowledged problem of suppression of negative findings from clinical trials sponsored by pharmaceutical companies.⁶⁰⁸ It has also been suggested that there is a particular risk of bias towards the reporting of positive results in the field of neurostimulation research.⁶⁰⁹ This is thought to arise because the ongoing lack of clarity about exactly *how* neurostimulation achieves its effect encourages the publication of *any* incidental positive results, even if these were not part of the original research protocol and findings relating to the primary aims of the study were not positive. There is also anecdotal evidence that, in some research studies of non-invasive brain-computer interfaces (BCIs), participants who are found not to produce the requisite or kinds of readable brain signals will be excluded from the research sample at an early stage.⁶¹⁰ The exclusion of ‘non-responders’ means that resultant findings may be more positive than they might otherwise have been about participants’ capacities to control computer commands.

- 6.15 These practices run contrary to the ideals of RRI by failing to represent the true capacities and promise of neurotechnologies. It is, therefore, crucial that exclusions of participants, the original hypothesis being tested, disappointing negative findings, and commercial interests are made explicit in published research. Open science is now widely recognised as an important route towards supporting innovation that serves the public good.⁶¹¹ The registers of clinical experience that we recommended in Chapter 5 would help to contribute to this, and in Chapter 7, we consider the need for enhanced information governance in respect of neurodevices.

Continuous reflexive evaluation

- 6.16 RRI also requires that those pursuing or supporting research lift their eyes above the narrow focus upon a particular application of neurotechnology to ask first whether it will offer real advantages over existing therapies, and second what spin-off developments from a technology might be anticipated. Addressing these questions may help to avoid ‘lock in’ to a development trajectory that might not deliver socially beneficial ends.⁶¹² They may also help to illuminate the intermeshed nature of therapeutic technologies and their potential non-therapeutic applications – for example, the use of BCI-controlled games for both pure recreational activities and as useful tools to maintain the interest and engagement of users during the training phase of therapeutic or assistive uses of BCIs. This may be of particular value in assisting developers to anticipate, and if necessary protect against, the possible dual-uses of technologies for both benign and hostile ends. We discuss the issues raised by non-therapeutic applications in more detail in Chapter 8.

⁶⁰⁸ This has led to a campaign for all trials to be registered and their full methods and results reported: All Trials (2013) *All trials registered: all results reported*, available at: <http://www.alltrials.net/>. Lexchin JR (2005) Implications of pharmaceutical industry funding on clinical research *The Annals of Pharmacotherapy* **39**(1): 194-7.

⁶⁰⁹ Schlaepfer TE and Fins JJ (2010) Deep brain stimulation and the neuroethics of responsible publishing *The Journal of the American Medical Association* **303**(8): 775-6.

⁶¹⁰ See, for example, Friedrich EVC, Scherer R, Sonnleitner K and Neuper C (2011) Impact of auditory distraction on user performance in a brain-computer interface driven by different mental tasks *Clinical Neurophysiology* **122**(10): 2003-9; Höhne J, Schreuder M, Blankertz B and Tangermann M (2011) A novel 9-class auditory ERP paradigm driving a predictive text entry system *Frontiers in Neuroscience* **5**(99): 1-10; Horki P, Solis-Escalante T, Neuper C and Müller-Putz G (2011) Combined motor imagery and SSVEP based BCI control of a 2 DoF artificial upper limb *Medical & Biological Engineering & Computing* **49**(5): 567-77; Popescu F, Fazli S, Badower Y, Blankertz B and Müller K-R (2007) Single trial classification of motor imagination using 6 dry EEG electrodes *PLoS ONE* **2**(7): 1-5.

⁶¹¹ The Royal Society (2012) *Science as an open enterprise*, available at:

http://royalsociety.org/uploadedFiles/Royal_Society_Content/policy/projects/sape/2012-06-20-SAOE.pdf.

⁶¹² See: Nuffield Council on Bioethics (2012) *Emerging biotechnologies: technology, choice and the public good*, available at: http://www.nuffieldbioethics.org/sites/default/files/Emerging_biotechnologies_full_report_web_0.pdf, pp.16-17.

- 6.17 Challenging developers of neurostimulation devices to consider possible new directions for these technologies might seem unnecessary in a field of research where new neural targets for stimulation and new clinical indications are continually being sought for existing devices. But these might still be viewed as following a linear approach to anticipating opportunities and risks. Technology ‘foresight’ exercises alone are unlikely to be sufficient to anticipate potential directions of development because complex neurotechnologies can be expected to follow multifaceted and non-linear innovation trajectories.⁶¹³ This is likely to encompass a variety of actors, any of whom may assume the role of enactor of innovation development and uptake.⁶¹⁴ RRI of neurotechnologies require a truly reflexive approach to ongoing evaluation in which alternative development pathways are recognised and humility is exercised through a willingness to change direction in light of emerging evidence.⁶¹⁵ Humility is also required to recognise the developers and regulators cannot be alone in determining the direction of innovation; responsiveness to public views and values is an essential part of any evaluation.⁶¹⁶ The value of reflexive evaluation does not end at the point at which a neurotechnological application receives regulatory approval to enter the market, but endures with the responsibility to respond to unexpected adverse effects or emerging ‘off-label’ uses.
- 6.18 It is important not to overlook the role that regulatory or governance oversight can themselves play in helping to shape or constrain the trajectory of innovation in a technological sphere. The one-dimensional view that technology itself is the principal driver of change has long since been abandoned.⁶¹⁷ In recent decades, we have come to understand that science, technology and society co-produce our technological futures, greatly complicating the task but also giving us better insight into the kinds of considerations that must be taken into account if we are to plan better for such futures.⁶¹⁸ *Legal* foresighting has been defined as “the identification and exploration of possible and desirable future legal or quasi-legal developments aimed at achieving valued social and technological ends.”⁶¹⁹ It is, however, a nascent discipline: law can have an important role to play in the social-shaping exercise that foresighting encourages, but humility teaches us that it should be seen as only one element in the armoury of possible social responses.

Coordinated interdisciplinary action

- 6.19 It is tempting to portray researchers in a particular field of technological development as a single cohesive community. This is rarely true, and the field of neurotechnology is no exception. Innovation in BCIs is particularly notable for its interdisciplinarity, spanning (but not limited to) engineers, neurosurgeons and psychologists.⁶²⁰ From an RRI perspective, this poses a set of risks associated with the “fragmentation in the understanding of the overall picture.”⁶²¹ This

⁶¹³ ‘Foresight’ here refers to an evidence based, future-directed approach to analysing the potential opportunities and risks posed by an emerging technology in order to inform policy. See, for example, Martin BR and Irvine J (1989) *Research foresight: priority-setting in science* (London: Pinter); Georghiou L (1996) The UK technology foresight programme *Futures* **28(4)**: 359-77.

⁶¹⁴ Fraunhofer Institute for Systems and Innovation Research (2003) *Annex 3: integrating technological and social aspects of foresight in europe (ITSAFE)*, available at: <http://www.supra.ed.ac.uk/Publications/annex3.pdf>; Swierstra T and Rip A (2007) Nano-ethics as NEST-ethics: patterns of moral argumentation about new and emerging science and technology *Nanoethics* **1(1)**: 3-20.

⁶¹⁵ STEPS Working Paper 32. Brighton: STEPS Centre (2009) *Direction, distribution and diversity! Pluralising progress in innovation, sustainability and development*, available at: <http://anewmanifesto.org/wp-content/uploads/stirling-paper-32.pdf>.

⁶¹⁶ Owen R, Macnaghten P and Stilgoe J (2012) Responsible research and innovation: from science in society to science for society, with society *Science and Public Policy* **39(6)**: 751-60, at page 755.

⁶¹⁷ SUPRA (2003) *ITSAFE project: intergrating technological and social aspects of foresight in Europe*, available at: http://www.supra.ed.ac.uk/Publications/ITSAFE_FINAL_REPORT.pdf, pp. 16-8.

⁶¹⁸ Jørgensen MS, Jørgensen U and Clausen C (2009) The social shaping approach to technology foresight *Futures* **41(2)**: 80-6.

⁶¹⁹ Laurie G, Harmon SH and Arzuaga F (2012) Foresighting futures: law, new technologies, and the challenges of regulating for uncertainty *Law, Innovation and Technology* **4(1)**: 1-33, at page 3.

⁶²⁰ Haselager P, Vlek R, Hill J and Nijboer F (2009) A note on ethical aspects of BCI *Neural Networks* **22(9)**: 1352-7, at page 1355.

⁶²¹ *Ibid.*, at page 1355.

potentially leads to gaps in a global understanding of the technology’s capabilities, creates challenges for assigning responsibility (for example, for obtaining informed consent), threatens the effective dissemination of information (both within teams and to the media), and thus presents obstacles to assessments of efficacy and safety.⁶²² In addition, uncertainties generated by divergent development trajectories and the priorities and vision of diverse actors make directing regulatory and governance responses all the more challenging. Governance approaches that support all the elements of RRI that we outline here need to speak to many different actors and to unite their diverse endeavours under the common aim of promoting the well-being of those who will use the technologies.

- 6.20 However, this diversity is also valuable insofar as it offers multiple perspectives from which reflexive evaluation and the identification of valuable research directions may be undertaken, and should be embraced.⁶²³ There can also be significant value in different groups of actors working together to deliver outcomes that might not be so readily achieved in isolation. For example, collaborative, interdisciplinary efforts to gather and disseminate information might help to fill important evidence gaps in understanding the capabilities and unintended effects of neurodevices.

Effective and proportionate oversight

- 6.21 Here we understand ‘oversight’ to include a range of measures, including regulatory regimes, the common law, and governance approaches such as professional codes of conduct. There is a wealth of literature and debate on what is meant by ‘regulation’ and ‘governance’ in the context of biotechnologies.⁶²⁴ It is not possible to explore the contours of this in any depth in this report but the broad definition adopted here is that oversight encompasses systems or approaches of directing or influencing behaviours in science and innovation trajectories towards desirable public goods and away from undesirable social outcomes.
- 6.22 Before we turn our attention in Chapter 7 to the specific questions of how the regulatory framework that applies to novel neurotechnologies measures up against the elements of RRI outlined above, it will be useful first to consider the more fundamental matter of what good governance and regulatory approaches themselves look like in the context of these technologies. Our ethical framework is a valuable guide to addressing this question. The role for ethical analysis in the context of regulation and governance is in providing common language and the means to reflect critically on the processes involved, and to evaluate them relative to our core social values. The aspiration towards good governance and regulation in this area is an ethical issue because failures or limitations in these regimes will impact very seriously and negatively on core human and social interests.

Responsible oversight in a context of uncertainty

- 6.23 A well-functioning regulatory system would be expected to deliver safe innovations in a timely fashion and with a minimum of regulatory burden so long as considerations of safety and proportionality are met. As we have noted, a key hurdle here to assuring safety is uncertainty surrounding the unintended and long-term risks of novel neurotechnologies.
- 6.24 Regulators constantly face uncertainty about the future. It has been posited that society’s diverse feelings about new technologies – whether they are greeted with fear or hope – depends to some degree on “how confident we feel about our ability to regulate them and, indeed, on how we react to the prospect of being regulated by them” and that negotiating mixed

⁶²² Ibid, at page 1355; Mak JN and Wolpaw JR (2009) Clinical applications of brain-computer interfaces: current state and future prospects *IEEE Reviews in Biomedical Engineering* 2: 187-99 pp. 197-8.

⁶²³ Stirling A (2011) Pluralising progress: from integrative transitions to transformative diversity *Environmental Innovation and Societal Transitions* 1(1): 82-8.

⁶²⁴ See, for example, Lyall C, Smith J and Papaioannou T (2009) *The limits to governance: the challenge of policy-making for the new life sciences* (Farnham: Ashgate Publishing Limited).

perceptions of promise and threat is not an easy task for regulators.⁶²⁵ This then demands the question of *how* society can regulate in circumstances of uncertainty, especially when this coexists in tension with need and in competition with hype. We have suggested that uncertainty gives rise to a principle of caution; that we should be circumspect as to the paucity of evidence about longer-term and unintended effects of intervening in the brain when proceeding with neurotechnological development. This recommends an approach to regulation that instantiates this principle. Crucially, however, is not precisely the same as adopting the *precautionary principle* itself.

- 6.25 The precautionary principle is a central feature of European regulatory frameworks and many national systems.⁶²⁶ It is considered to sit “at the heart of medical and public health theory and practice and is an underpinning to many our current environmental and public health policies”.⁶²⁷ The precise definition of the precautionary principle is a contested matter. Some readings frame it as an approach to risk management.⁶²⁸ It is intended to allow actors and governments to proceed when faced with an absence of conclusive or unambiguous scientific knowledge about likely risks associated with a particular development, initiative, new project or product.
- 6.26 However, as we have already noted in introducing the principle of caution in Chapter 4 (see paragraph 4.23), the precautionary principle is often constructed in ways that may be seen to stifle innovation and be overly restrictive. A common criticism is that it fails to take account of the harms of *inaction* – in this context, the harms of failing to deliver effective therapeutic interventions.⁶²⁹ In contrast, an approach based in the principle of caution and the virtue of humility acknowledges that there are limits to evidence based approaches to scientific and policy development. The challenge of uncertainty arises not only from a lack of evidence, but also ambiguities in that which is available to us. As the National Institute for Health and Care Excellence (NICE), has observed: “All evidence requires interpretation as evidence alone cannot determine the content of a recommendation”.⁶³⁰ This leads to a conclusion that both scientific and non-scientific values should form part of decision-making when faced with uncertainty about how best to proceed.⁶³¹ Moreover, the virtue of responsibility also requires approaching innovation in a way that avoids lock-in and leaves open the possibility of reversibility or adopting a different path.

⁶²⁵ Bekou O and Murphy T (2010) Editorial *Human Rights Law Review* **10(4)**: 597-9, at page 597.

⁶²⁶ Annex III to the *European Council Resolution on the Precautionary Principle*, SN 400/00 ADD 1 20 EN, at paragraphs 24-5. See also: European Court of Justice Case C–236/01, *Monsanto Agricoltura Italia SpA and Others v Presidenza del Consiglio dei Ministri and Others*, ECR 2003 I–08105 (133), in which the ECJ stated that the principle is “...an integral part of the decision-making process leading the adoption of any measure for the protection of human health.”

⁶²⁷ Tickner J and Kriebel D (2006) The role of science and precaution in environmental and public health policy, in *Implementing the precautionary principle: perspectives and prospects*, Fisher E, Jones JS, and Schomberg Rv (Editors) (Cheltenham: Edward Elgar Publishing Limited). See also: Kopelman LM, Resnick D and Weed DL (2004) What is the role of the precautionary principle in the philosophy of medicine and bioethics? *The Journal of Medicine and Philosophy* **29(3)**: 255-8.

⁶²⁸ For example, according to Principle 15 of the Rio Declaration on Environment and Development (1992), “In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation”.

⁶²⁹ See, for example, Sunstein CR (2002) The Paralyzing principle *Regulation* **25**: 32-7.

⁶³⁰ NICE (2009) *Methods for the development of NICE public health guidance (second edition)*, available at: <http://www.nice.org.uk/media/2FB/53/PHMethodsManual110509.pdf>, at page 118.

⁶³¹ The Nuffield Council on Bioethics’ report ‘*Public health: ethical issues*’ addressed the role and value of precaution when the evidence for proceeding with particular policies is incomplete, fragmented or contested. Preference was given to the term ‘precautionary approach’ rather than ‘precautionary principle’, in recognition of the fact that multiple principles and considerations must be taken into account. See: Nuffield Council on Bioethics (2007) *Public health: ethical issues*, available at: <http://www.nuffieldbioethics.org/sites/default/files/Public%20health%20-%20ethical%20issues.pdf>, at page xviii. The emphasis on the principle of caution we adopt in the present report is similarly motivated.

Proportionality in a context of need

- 6.27 Caution alone cannot be the only guide to effective regulation. The concept of need that lies at the heart of our ethical framework, and the associated virtue of inventiveness, draw our attention to the risk that too much regulatory burden or governance in these processes can stifle research and innovation or create unacceptable delays, thus potentially denying access to treatment or assistance. A responsibility for proportionate oversight is owed to all parties affected by the development of novel neurotechnologies. This means not only patients, but also researchers, innovators, manufacturers and those with a wider economic interest in the design and delivery of safe and effective new inventions. The regulatory system must work well for all: it must not only be safe and effective, but it must also be efficient and proportionate to the risks and benefits involved. An inefficient and overly-burdensome regulatory system is not in anyone's interests and is unethical as a result.
- 6.28 Moreover, in an area of technological development that is characterised by uncertainty, efforts to control research and clinical practices must themselves instantiate humility in recognising that the optimal path will not always be obvious. One key aspect of this will be recognising the limits of what can be achieved by top-down regulation and identifying those areas where professional groups of actors may more usefully govern their own activities according to the relevant virtues and interests at stake.

Box 6.1: Regulatory principles

Three regulatory principles may be seen as relevant to achieving effective and proportionate oversight.

Proportionality is a central feature of European and domestic regulatory practice.⁶³² It provides an important safeguard against regulatory burden by requiring that the content and form of any particular action or policy must not go beyond what is necessary to achieve the regulatory objective, which must itself be proportionate to the benefits, risks, and alternative courses of action.⁶³³ This principle, therefore, also speaks against unjustified overlap between regulatory and governance regimes – for example, in clinical research where research ethics approval, regulatory compliance, good clinical governance and both product and device regimes must all be satisfied.

Subsidiarity relates to the question of who has responsibility for acting where multiple actors have competence at various strata of regulation and lines of accountability are unclear. It has particular salience in the European context, The European Commission has clarified that, where the European Union (EU) and Member States share competence, the principle of subsidiarity establishes a presumption in favour of the Member States taking action.⁶³⁴ This is relevant in the field of novel neurotechnologies, where Member States and the EU share competence in respect of the regulation of medical devices and advanced therapeutic medicinal products. The EU has sought to achieve harmonisation in these fields in response to its twin aims of ensuring safety and proper functioning of the internal market. In Chapter 7, we consider whether these aims might be inadequate to meet priorities in respect of novel neurotechnologies, leaving areas where the UK might consider acting to fill any regulatory gaps.

Regulatory orientation is concerned with the transparency and clarity of regulatory objectives. One caricature is that regulatory regimes are burdensome bureaucracies more concerned with form-filling than the advancement of human knowledge and well-being. In reality, regulators are committed to reducing burden and to the twin objectives of protecting research participants and patients while promoting scientific advancement. However, there is only so much that states can achieve alone through regulatory regimes if there is not commitment and buy-in from the communities being regulated. Early and sustained dialogue and interaction with stakeholders can help to ensure that regulation is most effectively oriented to predict, shape and protect against harms from possible directions of development.⁶³⁵

⁶³² Article 5 of the Official Journal of the European Union (2012) *The treaty on European Union*, available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2012:326:FULL:EN:PDF>; EUROPA (2012) *Glossary: proportionality principle*, available at: http://europa.eu/legislation_summaries/glossary/proportionality_en.htm.

⁶³³ European Commission (2010) *Report from the commission on subsidiarity and proportionality (18th report on better lawmaking covering the year 2010)* available at: http://ec.europa.eu/governance/better_regulation/documents/com_2011_0344_en.pdf.

⁶³⁴ *Ibid.* pp.1-2.

⁶³⁵ Fins JJ, Schlaepfer TE, Nuttin B *et al.* (2011) Ethical guidance for the management of conflicts of interest for researchers, engineers and clinicians engaged in the development of therapeutic deep brain stimulation *Journal of Neural Engineering* **8(3)**: 1-6.

Humility and limits of regulation

- 6.29 Even once the principles listed in Box 6.1 have been taken into account, the suitability of hard law and top-down, command-and-control response to fill regulatory gaps might still be questioned. Responsibility, and liability for harmful outcomes, can be attributed through law and regulatory frameworks and this can serve to foster a compliance culture where regulatory requirements become the main drivers of processes. While it is important that regulation embodies clear lines of accountability, this can have the unlooked-for consequence of creating burdensome bureaucracy and can result in losing sight of the underpinning ethical objective and values of the regime to deliver safe and effective products efficiently.
- 6.30 Humility counsels against a presumption that introducing more law or further layers of regulatory oversight is always the most appropriate response to any concerns we might have about the ethical and social impacts of novel neurotechnologies. This is particularly so in the context of the provision of novel neurotechnologies for therapeutic purposes. Knee-jerk, rapid regulatory responses can not only be ineffective but can prevent the emergence of the kinds of evidence and experience that are necessary to conduct an appropriate assessment of the advent and acceptability of a new technology. It also challenges us to consider when regulation is appropriate at all, and in whom this power ought to be vested.
- 6.31 In some circumstances, governance approaches (rather than regulation) will offer the most appropriate paradigm within which to respond to any concerns we might have about the conduct of research and innovation in the field of neurotechnology. The distinction between regulation and governance is not rigid; they overlap both in form and function. Nevertheless, governance from within a profession or community of professions involved in the development of new technologies offers some advantages over the external imposition of regulations. This is due to the fact that it permits responsible research and innovation to be undertaken as a collective endeavour, built upon iterative, flexible, reflective and consensual approaches that seek to engage actors at all stages of the innovation trajectory, regardless of the path that is taken.
- 6.32 In Chapter 7, we address the specific questions of whether the existing regulatory regimes that apply to medical devices and to stem cell therapies meet criteria for effective and proportionate oversight. In doing so, we ask, in particular, whether these regimes foster the kinds of practices and outcomes that we have identified as priorities for RRI in the field of novel neurotechnologies.