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When Is Human?

Rethinking the Fourteen-Day Rule

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37.1 INTRODUCTION

The processual, rapidly changing nature of the early stages of human life has provided recurring challenges for the way in which we legally justify the use of embryos *in vitro* for reproduction and research. When the latter was regulated under the Human Fertilisation and Embryology Act 1990 (as amended) ('the HFE Act'), not only did regulators attempt to navigate what we should or should not do at the margins of human life, but they also tried to navigate the various thresholds that occur in embryonic and research processes. In doing so, the response of law-makers was to provide clear-cut boundaries, the most well-known of these being the fourteen-day rule.[1]

This chapter offers an examination of this rule as a contemporary example of an existing mechanism in health research that is being pushed to its scientific limits. This steadfast legal boundary, faced by a relatively novel challenge,[2] requires reflection on appropriate regulatory responses to embryo research, including the revisitation of ethical concerns, and an *examination* of the acceptability of carrying out research on embryos for longer than fourteen days. The discussion below does not challenge the fourteen-day rule, or research and reproductive practices *in vitro* more generally *per se*, but rather explores the ways in which law could engage with embryonic (and legal) processes through attention to thresholds (as a key facet of these processes). This framing has the *potential* to justify extension, but not without proper public deliberation, and sound scientific and ethical basis. The *deliberation* and *revisitation* – not necessarily the revision – of the law is the key part to this liminal analysis.

To begin, this chapter gives an overview of how the fourteen-day rule came into fruition, before going on to summarise the research, published in early 2017, that has given rise to new discussions about the appropriateness of the rule, twenty-seven years after it first came into force. Thereafter, the rest of the chapter builds on the theme of 'processes' from Part I of this volume, and asks, briefly: what might we gain from thinking beyond boundaries in this context? Moreover, what might doing so add to contemporary ethical, legal and scientific discourse about research on human embryos? I argue that recognising the inherent link between processes and the regulation of the margins of human life, enables us to ask more nuanced questions

[1] Human Fertilisation and Embryology Act 1990 (as amended), s3(4).

[2] A. Deglincerti, et al., 'Self-organization of the In Vitro Attached Human Embryo', (2016) *Nature*, 533(7602), 251; M. Shahbazi et al. 'Self-organization of the Human Embryo in the Absence of Maternal Tissues', (2016) *Nature Cell Biology*, 18(6), 700–708.

about what we want for future frameworks, for example, '*when* is human?',[3] one that legal discussion often shies away from. Instead I will argue that viewing regulation of embryo research as an instance of both processual regulation and regulating for process has the potential to disrupt existing regulatory paradigms in embryo research, and enable us to think about how we can, or perhaps whether we should, implement lasting frameworks in this field.

37.2 BEHIND THE FOURTEEN-DAY RULE: THE WARNOCK REPORT, AND A 'SPECIAL STATUS'

The fourteen-day time limit on embryo research is of global significance. It is one of the most internationally agreed rules in reproductive science thus far,[4] with countries such as the UK, the USA, Australia, Japan, Canada, the Netherlands and India all upholding the rule in their own frameworks for embryo research[5] The catalysts for the implementation of the rule into many of these public policies are often accredited to two key reports:[6] the US Report on embryo research of the Ethics Advisory Board to the Department of Health, Education and Welfare,[7] and the UK report of the Warnock Committee of Inquiry into Human Fertilisation and Embryology.[8] This chapter will focus on the latter.

In 1984, the Warnock Committee published the Report of the Committee of Inquiry into Human Fertilisation and Embryology, also known as 'the Warnock Report'. This deliberative, interdisciplinary process was a keystone to law-making in this area in the UK. As a direct result of these deliberations, the use and production of embryos *in vitro* is governed by the HFE Act. This Act, which stands fast over thirty years later, brought legal and scientific practice out of uncertainty – due to the lack of a statutory framework for IVF and research pre-1990 – to a new state of being where embryos can be used, legally, for reproductive and research purposes under certain specified circumstances.

The Warnock Report was quite explicit that it was not going to tackle questions of the meaning of human 'life' or of 'personhood'. Instead, it articulated its remit as 'how it is right to treat the human embryo'.[9] The Report examined the arguments for and against the use of human embryos for research. Here, the Committee noted the plethora of views on the embryo's status, evidenced by the submissions received prior to the Report. They discussed each position in turn, before concluding that while the embryo deserves some protection in law, this protection should not be absolute. Notably, the source of this protection is not entirely clear from the Report. It cited the state of law at the time, which afforded some protection to the embryo, but not absolute protection.[10] Nonetheless, one can glean from their recommendations that this protection is sourced – at least in part – by virtue of embryos membership of the human species.

[3] For some, embryos are inherently 'human', and this chapter does not intend to support or negate this case.
[4] J. Appleby and A. Bredenoord, 'Should the 14-day Rule for Embryo Research Become the 28-day Rule?', (2018) *EMBO Molecular Medicine*, 10(9), e9437.
[5] I. Hyun et al., 'Embryology Policy: Revisit the 14 day Rule', (2016) *Nature*, 533(7602), 169–171.
[6] S. Chan, 'How and Why to Replace the 14-Day Rule', (2018) *Current Stem Cell Reports*, 4(3), 228–234.
[7] Ethics Advisory Board, 'Education and Welfare. Report and Conclusions: HEW Support of Research Involving Human In Vitro Fertilization and Embryo Transfer', (Department of Health, Education and Welfare, 1979).
[8] Committee of Inquiry into Human Fertilisation and Embryology, 'Report of the Committee of Inquiry into Human Fertilisation and Embryology', (Department of Health and Social Security, 1984), Cmnd 9314, 1984, (hereafter 'Warnock Report').
[9] Ibid., 11.9.
[10] Ibid., 11.16.

It is important to note that the Warnock Report did not explicitly answer the question of 'when does life begin to matter morally?', but rather considered the viewpoints submitted and 'provide[d] the human embryo with a special status without actually defining that moral status'.[11] Thus, in the HFE Act's first iteration,[12] not only did regulators attempt to navigate what we should or should not do at the margins of human life, but also the rapidly changing nature of those margins. The regulatory response to this has been to provide clear-cut boundaries surrounding what researchers can and cannot do, in reference to embryos *in vitro*, the most well known of these being the subject of this chapter, the fourteen-day rule, as contained in s3(4) of the HFE Act. The rule reads as follows:

3. Prohibitions in connection with embryos.
   (1) No person shall bring about the creation of an embryo except in pursuance of a licence.
   . . .
   (3) A licence cannot authorise—
      (a) keeping or using an embryo after the appearance of the primitive streak,
      (b) placing an embryo in any animal
      (c) keeping or using an embryo in any circumstances in which regulations prohibit its keeping or use,
   (4) **For the purposes of subsection (3)(a) above, the primitive streak is to be taken to have appeared in an embryo not later than the end of the period of 14 days beginning with the day on which the process of creating the embryo began, not counting any time during which the embryo is stored.** [emphasis added]

This section of the HFE Act also introduced the subsection that famously embodies the Warnock Report's abovementioned 'compromise position', which affords human embryos some 'respect'. It placed a clear *boundary* to the process of research: it is illegal to carry out research on an embryo beyond fourteen days, or after the primitive streak has formed, whichever occurs sooner. After that, the embryo cannot be used for any other purpose, and must be disposed of. In other words, as discussed further below, if decidedly an embryo created and/or used for research purposes, it may only ever be destroyed at the end of the research process.

Why fourteen days? The rule is based upon the evidence given to the Warnock Committee that it is around this stage that the 'primitive streak' tends to develop. It is also the approximate stage at which the embryonic cells can no longer split and thus produce twins or triplets, etc.[13] It was thus felt that this stage was morally significant, reinforced by the belief that this was the earliest known moment when the central nervous system was likely to have formed. This stage also marks the beginning of gastrulation, the process by which cell differentiation occurs. At the time, it was seen as a way to avoid, with absolute certainty, anyone carrying out research on those in the early stages of human life with any level of sentience or ability to experience pain.[14,15] In this way, as a reflection of the Committee's recommendations, embryos *in vitro* are often described as having a 'special status' in law; not that of one with personhood – attained at birth –

[11] N. Hammond-Browning, 'Ethics, Embryos and Evidence: A Look Back at Warnock', (2015) *Medical Law Review*, 23 (4), 588–619, 605.
[12] Human Fertilisation and Embryology Act 1990.
[13] P. Monahan, 'Human Embryo Research Confronts Ethical "Rule"', (2016) *Science*, 352(6286), 640.
[14] Nuffield Council on Bioethics, 'Human Embryo Culture', (Nuffield Council on Bioethics, 2017).
[15] It is worth noting that in 2017 Hulbert et al. found that there are no sensory systems or functional neural connections in embryos at the twenty-eight-day stage. For more discussion on this see Appleby and Bredenoord 'The 14-day Rule'.

but still *protected* in some sense. This in and of itself may be described as recognising the processual; it is implicit in the Committee's efforts to replicate a somewhat gradualist approach that recognises embryonic development – and any 'significant' markers within it.

While many would agree that a 'special status' in law results from this rule, the word 'status' – or any other of similar meaning – does not appear at all in the HFE Act (as amended) in reference to the embryo. It is clear, however, that the recommendations of the Warnock Report, made in light of its proposal for a 'special status', are reflected in this steadfast piece of legislation to this day, operationalised through provisions such as the fourteen-day rule.

Despite their contentions (see above), the Committee can arguably be understood as *implicitly* having answered the question of '*when* life begins to matter', by allowing research up to a certain stage in development.[16] In other words, they prescribed that 'as the embryo develops, it should receive greater legal protection due to its increasing moral value and potential'.[17] This policy, known as the gradualist approach, is somewhat in line with the Abortion Act 1967, which affords more protection to the fetus as it reaches later stages in development[18] (although in other ways these laws do not align at all). In doing so, while not explicit, the Act captures the processual aspect of embryonic/fetal development.

It seems that the human embryo hovers between several normative legal categories, i.e. 'subject' and 'object'.[19] While it clearly does not have a legally articulated 'status' under the HFE Act, it occupies a legal – and for some people, moral – threshold between all of these aforementioned categories, which we can see by the special status it has been given in law. Thus, while there is no explicit legal status of the embryo, what we have, legally, is still *something*. By virtue of giving the embryo *in vitro* legal recognition, with attached allowances and limits, it arguably has a status of sorts. Bearing in mind that the law adopted most of the Warnock Report's recommendations, its status may indeed be described as 'special', as the Report prescribed. It is 'not nothing',[20] yet not a 'person': it is the quintessential liminal entity, betwixt and between. From what we have seen, its status remains 'special', the meaning of which is unclear except that it is afforded 'respect' of sorts. Beyond that, we can glean little regarding what the extent or nature of this from domestic law is. It does not have an explicit legal status, but, as some argue, it may have one implicitly.[21] This begs the question: what does it mean to have 'legal status'? Is it enough to be protected by law? Recognised by law? Entitled to something through law? These are the types of questions we may want to consider for any amendments, or new frameworks, going forward.

37.3 BEYOND FOURTEEN DAYS?

As we have seen, the fourteen-day rule is the key legal embodiment of the embryo's decidedly 'special status' and the application of a legal and moral boundary at the earliest stages of human life. Yet throughout the incremental amendments to the HFE Act (e.g. the HFE Act 2008), there has been little enthusiasm among policy-makers for revisiting, let alone revising, the rule. For some, the latter did not necessarily matter, as, for twenty-seven years, this limit was 'largely

[16] Hammond-Browning 'Ethics, Embryos and Evidence', 604.
[17] Ibid., 605.
[18] See Abortion Act 1967, s1.
[19] See C. McMillan et al., 'Beyond Categorisation: Refining the Relationship between Subjects and Objects in Health Research Regulation', (2021) Law, Innovation and Technology, doi: 10.1080/17579961.2021.1898314.
[20] *St George's Healthcare NHS Trust* v. S [1998] All ER 673, [1998] 3 WLR 936, 952.
[21] Hammond-Browning 'Ethics, Embryos and Evidence', 606.

theoretical';[22] up until very recently, no researcher had been able to culture an embryo up to this limit.

In early 2016, for the first time, research published in *Nature*[23] and *Nature Cell Biology*[24] reported the successful culturing of embryos *in vitro* for thirteen days. With the possibility of finding out more about the early stages of human life beyond this two-week stage, calls have been made to revisit the fourteen-day rule.[25] Why? It appears that some valuable scientific knowledge may lie beyond this bright legal line in the sand, within this relatively unknown 'black box of development'. For example, it would enable the study of gastrulation, which begins when the primitive streak forms (around fourteen days).[26]

Yet what might all of this mean for compromise, respect, and the resulting 'special' legal status of the embryo? If this rule were to change, would the embryo still be 'special'? Moreover, do we believe this matters? These questions should be addressed if we revisit the rule; it seems that discussions surrounding the fourteen-day rule are part of a broader issue that needs to be addressed. There is a very strong case for public and legal discourse on the meaning and 'special' moral status of the embryo in UK law. One question that we may want to revisit is: if we value the recommendations of the Warnock Committee ('special', 'respect', etc.), does it still have resonance with us today? For example, one might ask: even if the 'special' status has a justifiable source, how can we 'value' it in practice except by avoiding harm? It is arguable that the 'special respect' apparently afforded in law seems meaningless in practical terms.[27]

It is difficult to enable a 'middle position' between protection and destruction in practice; we either allow embryos to be destroyed, or we do not. For some, the embryo's 'special status' is thus, arguably, purely rhetorical; it does not oblige us to 'act or refrain in any way'.[28] However, compromise is arguably more nuanced than allowing or disallowing destruction of embryos. Time is an essential component of legal boundaries within the 1990 Act (as amended). Either one can research the embryo for less than fourteen days, or one cannot. This means that we cannot research the embryo for any longer period of time, for example thirty days or sixty days. Rhetoric aside, the concept of the 'special status' is still very powerful and has acted as a tool to 'stop us in our tracks' with regards to research on embryos. It is arguably a precautionary position, which reflects that we as a society afford a degree of moral and legal value to embryos, and thus the special status caveat requires us to proceed cautiously, to reflect, to justify fully, to revisit, to revise and to continue to monitor as we progress scientifically. If we did not value the embryo at all, then we would have carte blanche to treat it however we wished. If that were the case, research at 30 or 60 or 180 days would not present a problem. Therefore, the embryo's special status need not be an all-or-nothing brake on research, nor a green light position. It thus means something in that sense, however (admittedly) meaningless. The 'special status', then, is – in a way – not a 'compromise', but what I would term a legal and ethical *comfort blanket*.[29]

This is not to criticise the language used by the Committee, however. The Warnock Committee's emphasis on 'compromise' was made in the name of moral pluralism. In other

[22] S. Chan, 'How to Rethink the Fourteen-Day Rule', (2017) *Hastings Center Report*, 47(3), 5–6.
[23] Deglincerti et al., 'Self-organization', 533
[24] Shahbazi et al., 'Self-organization of the Human Embryo', 700.
[25] Hyun et al., 'Embryology Policy', 169.
[26] Chan, 'How and Why', 228.
[27] See M. Ford, 'Nothing and Not Nothing: Law's Ambivalent Response to Transformation and Transgression at the Beginning of Life' in S. Smith, and R. Deazley (eds), *The Legal, Medical and Cultural Regulation of the Body: Transformation and Transgression* (London: Routledge, 2009), pp. 21–46.
[28] Ibid., 43.
[29] C. McMillan, *The Human Embryo in Vitro: Breaking the Legal Stalemate* (Cambridge University Press, 2021).

words, it emerged as the Warnock Committee's way of navigating the uncertainty/ambivalence surrounding how to treat embryos *in vitro*, legally. This is not to say that poles of opinion between which this compromise was set have changed. The rule, a reflection of this 'compromise' was, in many ways, a new boundary and threshold akin to its historical counterparts (such as quickening). Yet if we decide that it is worth considering this boundary and whether we want to change it, how can – or should – we rethink it? If we believe that the process embryonic and scientific development is a relevant factor in determining an appropriate regulatory response, what might further focus on these key points in transition bring to contemporary debates?

The rest of this chapter argues that if we want to think beyond the boundary of the fourteen-day rule, one way of framing discussion is by recognising the inherent link between processes and regulating of the margins of human life. When considering frameworks, the latter enables us to ask questions surrounding not only 'what is human?', but '*when* is human'? Asking '*when*?' – used here as an example – allows us to re-focus on not only embryonic development as process, but questions surrounding we need to place different boundaries within that process.

37.4 REVISITING THE RULE

Throughout the regulation of the early stages of human life, law has changed to reflect the changing boundaries of what is 'certain' and 'uncertain'.[30] Where new uncertainties arise,[31] some old ones will always remain.[32] We have thus moved, in some ways, from one type of uncertainty to another when it comes to embryo regulation, and this is because what we are dealing with is an inherently processual entity, that in and of itself has not changed. In other words, the complex and relatively uncertain nature of embryos, the stage of human life at which development occurs at its fastest pace, continues to cause widespread ambivalence[33] on how it is right to treat it.

When considering whether to alter the rule, multiple thresholds – such as the threshold for humanity – within embryonic and research processes come into consideration.[34] As we have seen, there was a strong nod to the gradualist approach in the thought behind the fourteen-day rule – an approach that recognises that human development is a process. The Report did not set out to answer '*when* is human?', but pointed to an important stage in the process of *becoming human*, when limiting research to fourteen days. As we have seen, the Warnock Committee used ethical deliberation and evidence available at the time to suggest this boundary beyond which research could not pass. A key part of this deliberation, although not referred to in terms of 'thresholds' *per se*, were particular (perceived) biological thresholds, such as the threshold for experiencing pain – which they associated with the start of the primitive streak – and thresholds for being able to cause harm therein. One might say that if the fourteen-day rule is a limit or a boundary, then something that we may want to consider – if we deem it appropriate to revisit this rule – is the presence of *thresholds* therein, and the importance that we want to attribute to those thresholds.[35] While being in a liminal state or space connotes occupying a threshold, a key part

[30] S. Taylor-Alexander et al., 'Beyond Regulatory Compression: Confronting the Liminal Spaces of Health Research Regulation', (2016) *Law, Innovation and Technology*, 8(2) 149–176; McMillan, 'The Human Embryo'.

[31] I.e. Should research and reproductive embryos be treated the same? Should the fourteen-day rule be extended? What can we find out about time between fourteen and twenty-eight days? Etc.

[32] I.e. The question of how we should treat embryos is, of course, never certain because there is no objective answer; in recognition of moral pluralism it is very much a subjective matter.

[33] See Ford, 'Nothing and Not Nothing', 31

[34] This is not to suggest that we could cross boundaries between research and reproduction, however.

[35] Taylor-Alexander et al., 'Beyond Regulatory Compression'.

of the liminal process is moving out of the liminal state, i.e. over or beyond that threshold. Thinking about liminal beings such as embryos in such terms highlights the presence of these boundaries and their potential for impermanence, especially in a legal context. For example, if we decide it is appropriate to *consider* extending the rule, these types of moral boundaries (i.e. harm, or sentience, etc.) may very well come into play again, for example if a 'twenty-eight-day rule' is proposed. Further, talks around extending it have already given rise to discussion surrounding another kind of boundary: would extending the rule be of adequate benefit to science? Some argue that there is much more that we can learn from extending the limit.[36] Yet, what amount of benefit is enough benefit to justify extension? Therein lies the threshold, a threshold of the reasonable prospect of sufficient scientific 'benefit'.

If the crossing of thresholds within biological and research processes have been implicitly important for us thus far, what might we learn from this? With regards to the legal processes that we *already have*, attention to process – and therefore thresholds – highlight the following:[37]

- Once an embryo created *in vitro* passes the threshold of being determinedly a 'research' embryo, it cannot (legally) be led back past the said threshold, and it can only come out this process as something to be disposed of after being utilised.
- In contrast, there are lots of thresholds that embryos are led through for a 'reproductive' path, for example: (non)selection after PGD, implantation, freezing and unfreezing, implantation, gestation etc. – indeed, this includes the possibility of crossing the threshold from 'reproduction' to 'research' if, say, PGD tests suggest non-suitability for reproduction.
- When the progenitors of embryos are making decisions regarding what to do with their surplus embryos, they may cross various thresholds themselves, e.g to donate or not, either for research or to others seeking to reproduce.

Regarding the last point, persons/actors are, of course, an essential part of these processes and this should not be lost in any renewed discussions surrounding the rule. Considerations for the actors around embryos can be different for each threshold, i.e. we may consider different sets of factors depending on which threshold any particular embryo is at. For example, at the third threshold above, many factors come into consideration for donors, including their attitudes towards research and their feelings about and towards their surplus embryos and their future (non)uses.[38] Moreover, each threshold is coupled with clear boundaries, be it the fourteen-day rule for 'research' embryos, or rules around what may/may not be implanted for 'reproductive' embryos.

Thresholds – or indeed boundaries – are not necessarily 'bad' here, per this work's analysis. Indeed, both moral and legal thresholds are of crucial importance. Rather, I suggest that we should be alive to their presence and their place among the broader network – of actors, or silos, etc. – in order to ask questions about the conditions we want in order to cross those thresholds.[39] As I have argued elsewhere: 'Considering the multiplicity, variability, and in many ways, subjectivity of these thresholds might enable us to regulate in a more flexible and context-specific way that allows us to recognise the multiplicity of processes occurring within the framework of the [HFE Act].'[40] Attention to process cannot necessarily say how any revisitation might turn out.

[36] E.g. S. Wong, 'The Limits to Growth', (2016) *New Scientist*, 232(3101), 18–19.
[37] See McMillan, 'The Human Embryo'.
[38] See E. Jonlin, 'The Voices of the Embryo Donors', (2015) *Trends in Molecular Medicine*, 21(2), 55–57; S. Parry, '(Re) Constructing Embryos in Stem Cell Research: Exploring the Meaning of Embryos for People Involved in Fertility Treatments', (2006) *Social Science and Medicine*, 62(10), 2349–2359.
[39] See McMillan, 'The Human Embryo'.
[40] Ibid.

It is important to revisit the intellectual basis for any law, but especially so in a field where technology and science advance so rapidly. If we do not, we cannot ask important questions in light of new information, for example: what or when is the threshold for 'humanity'? Or if indeed we want 'when is human' to factor into how we regulate embryos, as it has done in the past. Discussing questions such as these would be a great disturbance to the policy norm of the past twenty-seven years or so, which have stayed away from these types of questions. But I argue that within disturbance, we can find resolution through proper legal and ethical deliberation, and public dialogue. In other words, it would not be beneficial of us to shy away from disruptions for fear of practice being shut down, as these disturbances present us with a chance to feed experiences and lessons of those involved in – and benefit from – research back into regulatory, research, and – eventually – treatment practice.

37.5 CONCLUSION

While the time limit on embryo research has undoubtedly been a success on many fronts, if it is to remain 'effective and relevant',[41] we must be open to revisiting it, with proper deliberation and public involvement, with openness and transparency.[42] Not only that, but when doing so, we must not shy away from asking difficult questions if law is to adapt to contemporary research.

The latter part of this chapter has argued that a focus on process has the potential to disrupt existing regulatory paradigms in embryo research and enable us to think about how we can, or perhaps whether we should, implement lasting frameworks in this field. The above did not challenge the pros and cons of the fourteen-day rule, or research and reproductive practices *in vitro* more generally *per se*, but rather briefly explored one of the ways which law could engage with embryonic (and legal) processes through attention to thresholds (as a key facet of these processes).

Overall, while the framing offered here has the *potential* to justify an extension of the fourteen-day rule, it cannot be done without proper public deliberation. This deliberation would need to be subject to sound scientific objections, and perhaps most importantly, subject to scrutiny regarding prevalent moral concern over pain and sentience.[43] This analysis challenges us to *deliberate*, and *revisit* – not necessarily the revise – the law surrounding this longstanding rule. Responsive regulation, per the title of this section of the volume, need not respond to every 'shiny new thing' (e.g. advances in research, such as those discussed in this chapter), but be reflexive (and reflective) so that HRR does not become stagnant.

[41] Appleby and Bredenoord, 'The 14-day Rule'.
[42] G. Cavaliere, 'A 14-day Limit for Bioethics: The Debate over Human Embryo Research', (2017) *BMC Medical Ethics*, 18(38).
[43] See McMillan, 'The Human Embryo'.