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Generic or Specific? The Frames of Stem Cell Procurement Regulation in Europe

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Abstract

The procurement of stem cells, which is a crucial source-material in biomedical research promising the development of novel therapies in regenerative medicine, is subject to regulation using generic and technology-specific provisions throughout Europe. The relevant national regulatory regimes, while they share common regulatory frames, exhibit considerable differences as a matter of the regulatory approach followed, the biological level regulated, or of the context in which technologies for stem cell procurement are regulated. This variety indicates that legal regulation may resort to different means so as to secure a connection with the technology regulated. It is proposed that for improving "regulatory connection" states should consider engaging in regulatory borrowing from other systems covering both generic and specific instruments of technology regulation.

Keywords
stem cell regulation, legal regulation of stem cell procurement, regulatory connection, frames of regulation, national diversity, regulatory mixity, regulatory borrowing

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1 Introduction

Stem cell technologies, including the procurement of stem cells for research or for therapeutic purposes, are subject to fairly extensive regulation in Europe both at national and supranational level. Predominantly, the relevant regulatory instruments deal with questions which usually appear in the regulation of emerging biomedical technologies, such as risk, quality and safety, the ethics of biomedicine and biomedical research, or the achievement of public health objectives. Stem cell technology-specific measures, if they are available, address matters which have direct connection with the procurement and use of stem cells in biomedicine. The most frequently regulated is the determining of the permitted sources of stem cells. In most countries, these and other relevant regulatory frames are covered as integral parts of broader measures regulating generic areas, such as assisted reproduction, tissue and cell donation, or biomedical research. Only a few states have adopted instruments which are dedicated per se to stem cell technologies. These address certain issues prioritised in the local and European bio-legal discourse – for example, the availability of supernumerary human embryos for stem cell procurement – rather than regulating the technological domain comprehensively.

In this article, we examine the different regulatory regimes in Europe through the different frames they employ in regulating stem cell procurement. This comparative exercise is carried out to assess – considering the potential held by stem cell technologies in terms of future public health benefits, in particular their application in regenerative medicine – whether their regulation in stem cell technology-specific measures should be preferred over the use of general biomedical regulation. This issue bears relevance from the perspective of the broader dilemma specific to technology regulation, namely the ensuring of an adequate "connection" between rules and the technology regulated. The

diversity of provisions governing the relevant regulatory frames as revealed in this article indicates that, in their current state, the regulatory systems examined operate as mixed regimes offering different – both generic and specific – solutions, which in turn suggests the availability of multiple practices in securing the connection between stem cell technologies and the diverse rules applicable to them. On this basis, there may be a case for considering inter-systemic regulatory learning and borrowing provided that, having regard to the significant public health benefits promised, the connection between rules and stem cell technologies is sought to be improved by regulators.

This article is structured as follows. Firstly, it examines the broader basis in regulatory theory for comparing the regulatory frames as covered in the different systems of biomedical technology regulation in Europe, namely the dilemma of connecting rules with the technology regulated and the related issue of choosing between generic or specific provisions to secure regulatory connection. This is then followed by a comparative overview of the frames of stem cell technology regulation in different European states with a focus on the regulation of stem cell procurement. The article closes with an analysis of the regulatory variety and trends revealed by the comparative exercise having regard to the considerable diversity of solutions and practices. The legal material and ideas discussed in this work follow from the legal mapping report prepared in the *EUCelLEX* research project financed from the EU 7th Framework Programme, which examined and compared the regulation of stem cell procurement in Canada and a select group of states in Europe.[1]

[1] EUCelLEX: Cell-based regenerative medicine: new challenges for EU legislation and governance (Grant agreement no.: 601806), available at http://www.eucellex.eu (accessed 5 May 2017). The countries included were Austria, Belgium, Canada, France, Germany, Hungary, the Netherlands, and the United Kingdom. They were selected with a view to securing sufficient diversity in the research of national regulatory regimes. The scope of the project consequently determines the scope of analysis in this article.

2 Regulatory frames and technology regulation: A regulatory tango

When analysing the regulation of stem cell technologies and the technologies of stem cell procurement,[2] it must be borne in mind that this is a developing technological domain, which remains subject to debates and controversies from scientific, ethical and legal perspectives. In legal regulation, the area has given rise to an interesting, and from the perspective of the future of the technologies involved, crucial interplay between rules and the technologies regulated – akin to a dance of tango – which employs an exciting array of bio-legal constructions involving new terms, categorisations and entities. It is not only the widely discussed ethical implications which make the legal regulation of this domain challenging, but regulators – aiming to ensure that the rules are adequately connected to the technology regulated – also face considerable dilemmas when they select the terms and categorisations and develop, with their help, the frames of regulation.[3]

In this interplay, law and legal regulation participate with limited capabilities. Its desire to distinguish between the different components of the technology and accordingly set up categorisations assigning prohibitive or

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[2] It is important to note that we speak about stem cell technologies in plural, indicating that there are indeed multiple technologies in question which may raise very different issues requiring regulatory intervention. The emergence of human embryonic stem cell (hESC) technology meant that bioethical issues, which had no relevance for blood stem cells or adult stem cells, in particular the protection of human (embryonic) life, had to be addressed. The more recently discovered possibility of creating induced pluripotent stem cells (iPSC), which promises the replacement of hESC technology, was heralded as offering a way out from the moral dead end street of hESC technology. See, in this regard, Kristina Hug and Göran Hermerén, "Do We Still Need Human Embryonic Stem Cells for Stem Cell-based Therapies? Epistemic and Ethical Aspects" (2011) 7(4) *Stem Cell Reviews* 761-774.

[3] See the technological frames listed and the argument concerning a "fully inclusive approach" to regulating new health technologies, which means that regulation is effective and it is fully negotiated by all affected parties in Amanda Warren-Jones, "Mapping Science and New Health Technologies: in Search of a Definition" in Mark Flear, Anne-Maree Farrell, Tamara Hervey and Thérèse Murphy (eds.), *European Law and New Health Technologies* (Oxford: OUP, 2013) 70-102, pp. 70-71.

permissive rules to the components identified[4] is regularly confronted with resistance from scientific and technological developments to such formalised treatment.[5] There are many examples of technologies shaking off law's distinctions and putting pressure on the interpretation and application of corresponding rules.[6] In the US case *Flynn v Holder*,[7] the law responded to challenges posed by technology by introducing a distinction between bone marrow obtained through traditional aspiration and blood cells procured through apheresis, which from a technological point of view is at least dubious. The expansion in *Brüstle v Greenpeace*[8] by the European Court of Justice of the clause in European patent law prohibiting the industrial use of human embryos to cover embryonic stem cells was another controversial legal development not supported entirely by technological reality. The controversial deferential attitude from human rights law towards the recognition of the right of access to a last hope treatment when it is an unlicensed stem cell therapy revealed in the *Durisotto v Italy* decision of the European Court of Human Rights[9] indicates law's inability, perhaps unwillingness, to address issues raised by available technological possibilities.

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4 For instance, on the basis of their risks or ethical implications, the law will distinguish between acceptable and prohibited sources of stem cells, the different types of stem cells, or between the different uses of stem cells.

5 See also the Dutch proposal to allow the growing, under strict conditions, of human embryos beyond the generally applicable temporal restriction for the purposes of research on infertility, assisted reproduction and hereditary and congenital diseases available at https://www.theguardian.com/science/2016/may/28/netherlands-gives-green-light-for-growing-human-embryos (accessed 4 November 2016), which challenges the well-established and well-entrenched fourteen-day rule concerning the permissibility of research on human embryos, *infra* n. 53-56.

6 See also the UK House of Lords' judgment in *Quintavalle*, *infra* n. 91.

7 *Flynn v Holder,* 684 F. 3d 852 (9th Circ. 2012).

8 *Brüstle v Greenpeace*, Case C-34/10, ECLI:EU:C:2011:669. For an analysis, see Márton Varju and Judit Sándor, "Patenting Stem Cells in Europe: The Challenge of Diversity for EU Law" (2012) 49 *Common Market Law Review* 1007-1038.

9 *Durisotto v Italy*, Decision of 6 May 2014, App. No. 62804/13, nyr. (ECtHR). For a commentary, see Emmanuelle Rial-Sebbag and Alessandro Blasimme, "The European Court of Human Rights' Ruling on Unproven Stem Cell Therapies: A Missed Opportunity?" (2014) 23 Suppl 1 *Stem Cells Dev* 39-43.

With these uncertainties in mind, revisiting which regulatory frames are used by different regulatory regimes and how they – employing generic or technology-specific provisions regulating those frames – connect with the technology regulated is not only a justifiable, but also necessary exercise. In the stem cell domain, there are significant public health objectives at stake, as promised by the emerging biomedical area of regenerative medicine. Realising these should not be hindered by rules which are inadequately connected with the technology or with particular dimensions of that technology. The concept of connecting regulation to the technology in question was raised in the discourse in regulatory theory.[10] Its relevance was seen as being able to ensure that the "potential health, safety, environmental, social, ethical and regulatory issues" which may be raised by the technology in question are addressed, or alternatively that regulators are prepared to address these when they emerge.[11] It was suggested that for regulation to be able to fulfil this expectation it needs to demonstrate certain fundamental qualities, namely it has to be effective and meet the requirement of regulatory economy, and it has to be legitimate and democratic.[12] The discourse also raised that technology regulation, despite the different pressures arising in the context of making a connection with the technology regulated, must be able to uphold law's inherent values and the rule

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[10] The focus is on the correspondence between the legal text and its purposes and the forms and uses of the technology. See R Brownsword, "So What does the World Need Now? Reflections on Regulating Technologies" in Roger Brownsword and Karen Yeung (eds.), *Regulating Technologies: Legal Futures, Regulatory Frames and Technological Fixes* (Oxford: Hart, 2008) 23-48, at 26-27. See also Jasanoff's more general assessment of the "intersections" between law and science, especially the practices adopted by legal "experts" applying legal rules towards science and scientific development (in particular, the deference owed by law to science) in Sheila Jasanoff, *Science and Public Reason* (London: Routledge, 2012), pp. 15-18; Sheila Jasanoff, "Making Order: Law and Science in Action" in E J Hackett et al (eds.), *The Handbook of Science and Technology Studies* (Cambridge, MA: MIT Press, 2008) 761-786, pp. 761 and 768; and her work on the "co-production" of orders by law, science and technology in Sheila Jasanoff, "Ordering Life: Law and the Normalization of Biotechnology" (2001) 17(62) *Notizie di Politeia* 34-50.

[11] Brownsword and Yeung, *Regulating Technologies*, *supra* n. 10, p. 28.

[12] *Ibid.*, pp. 26-27.

of law itself.[13] Ultimately, regulation must be able to ensure that the relevant policy objectives are realised in an acceptable way. When the development of novel therapies serves as the aim of regulatory intervention, regulation must not prevent access, more importantly just and equitable access, of patients to those new therapeutic opportunities.[14]

The regulatory connection discourse, in analysing the problems of securing adequate connection, also touched upon the choice between generic and technology-specific rules in the regulation of the relevant regulatory frames. It did not propose definitive answers in this regard, rather it highlighted the dilemmas and pointed to the ongoing interplay between rules and the technology regulated.[15] It was claimed that, on the one hand, experiences with overly specific regulation indicate that generic regulatory approaches and the use of general regulatory frameworks may be better placed to govern emerging technologies.[16] Technological development and its inevitable unforeseeability were seen as

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13 See Sheila Jasanoff, "Serviceable Truths: Science for Action in Law and Policy" (2015) 93 *Texas Law Review* 1723-1749, pp. 1724-1725, concerning the ability of law to represent its inherent values, such as representation, order and stability, accountability, liberty and justice vis-à-vis science. For the broadest formulation of this problem, see the famous paradigm by Lessig that law's contribution to regulation (to establishing "the optimal mix" of regulatory modes) cannot be contradictory to law's specific ends in Lawrence Lessig, *Code and Other Laws of Cyberspace* (NY: Basic Books, 1999) pp. 222-223 and Lawrence Lessig, *Code Version 2.0* (NY: Basic Books, 2006) pp. 325-326. See also Brownsword and Yeung, *Regulating Technologies*, *supra* n. 10, p. 31 on the rule of law as a consideration which needs to be taken into account in the analysis of regulatory connection and see Jasanoff, *Science and Public Reason*, *supra* n. 10, pp. 15-18 and Jasanoff, "Serviceable Truths", *supra* n. 13, pp. 1724-1725 on her arguments concerning minimum deference in law towards science "where the law's core concerns for representation, accountability, and justice, as defined by legal norms, should take precedence over science's claims to higher authority".

14 See Hoppe's argument concerning the impact of overregulation and generally of inadequate regulation on equity and justice in the health care context in Nils Hoppe, *Bioequity – Property and the Human Body* (Farnham: Ashgate, 2009) and Nils Hoppe "Innovative Tissue Engineering and its Regulation – the Search for Flexible Rules for Emerging Health Technologies" in Mark Flear et al (eds.), *European Law and New Health Technologies* (Oxford: OUP, 2013) 109-124, p. 113.

15 Brownsword suggested that the pressure on regulators to connect regulation with technological developments, in a manner that ensures the effectiveness, efficiency, legitimacy and democratic nature of regulation, is likely to remain constant, in Brownsword and Yeung, *Regulating Technologies*, *supra* n. 10, p. 32.

16 *Ibid*., p. 30.

likely to lead to the clearest, most precise, and detailed measures losing connection with their "technological target".[17] On the other, it was suggested that there is no guarantee that generic regulation will satisfy expectations of adequate connection, as the distinctiveness of individual technologies may demand that we "refine our regulatory intelligence to bring (regulation) into alignment with the characteristics of each particular technology."[18] Regulators, thus, face constant pressure to experiment with approaches and regulatory solutions – both generic and technology-specific – having regard to the characteristics of the technology regulated and taking into account the aforementioned fundamental legal qualities of technology regulation.[19] On this basis, in domains such as stem cell technologies and technologies of stem cell procurement, current regulatory frameworks employing diverse regulatory frames should be open to improvement, potentially by learning and borrowing from other regimes.

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[17] *Ibid.*, p. 27. In this connection, see Brownsword discussing the dilemma of choosing between securing flexibility and ensuring consistency in regulation.

[18] *Ibid.*, p. 30.

[19] *Ibid.*, pp. 31-32. The synergies between the different factors must also be recognised. The effective regulation of the risks posed by the new technology may contribute significantly to the legitimacy of regulatory intervention. See in the EU context, where other sources of legitimacy, such as public trust, may be difficult to secure, Anne-Maree Farrell, "Risk, Legitimacy, and EU Regulation of Health Technologies" in Mark Flear et al (eds.), *European Law and New Health Technologies* (Oxford: OUP, 2013) 203-221, pp. 205-207.

Table 1. The national measures available to regulate stem cell procurement.

Austria	Act on Medically Assisted Reproduction	Act on Tissue Quality and Safety		
Belgium	Act on Medically Assisted Reproduction and on the Fate of Supernumerary Embryos and Gametes	Act on the Procurement and Use of Human Bodily Material for Medical Purposes and for Purposes of Scientific Research	Act on Research on In Vitro Human Embryos	
France	Public Health Code			
Germany	Embryo Protection act	Stem Cell Act	Transplantations Act	Transfusions Act
Hungary	Act on Health Care			

The Netherlands	Embryo Act	Foetal Tissue Act	Act on the Quality and Safety of Body Material	Act on Medical Research involving Human Subjects
United Kingdom	Human Tissue Act 2004	Human Fertilisation and Embryology Act 1990		

3 The frames of stem cell procurement regulation in Europe

The instruments (Table 1) which directly or indirectly regulate the procurement of stem cells in different states in Europe reveal a variety of frames connecting the rules with the technology. Although most regulatory frames are shared, partly as a result of EU regulation,[20] there can be considerable variation in the detail and focus of regulation, the regulatory approach selected, the biological level regulated, the scientific context or human activity regulated, and even in answering whether stem cell technologies and technologies of stem cell procurement should be considered as areas requiring targeted regulatory intervention.[21] The national measures are predominantly generic in their approach. The stem cell-specific norms, if available, were introduced in order to complement existing frameworks regulating general areas of biomedicine, such as assisted human reproduction. It is rare that stem cell procurement is regulated in self-standing rules in a separate instrument.

As is evident from Table 1, only a few of the national regulatory systems examined intervene at the level of stem cells, and even fewer at the level of hESC

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[20] The key measure is the generic Tissues and Cells Directive (Directive 2004/23/EC on Setting the Standards of Quality and Safety for the Donation, Procurement, Testing, Processing, Preservation, Storage and Distribution of Human Tissues and Cells, [2004] OJ L102/48), which regulates issues, such as risk, quality and safety, and the related institutional and procedural arrangements. The frames it introduced for regulation at the Member State level follow from its general objectives and from its dominant implementation paradigm (the market) aiming to secure the realisation of those objectives. These are public health protection, risk reduction and ensuring quality and safety, protecting rights and values, and maintaining national diversity. For the dominant regulatory frames in EU health technology regulation, which include markets, risk, and rights and ethics, see Gordon Bache, Mark Flear and Tamara Hervey, "The Defining Features of the European Union's Approach to Regulating New Health Technologies" in Mark Flear et al (eds.), *European Law and New Health Technologies* (Oxford: OUP, 2013) 7-45, pp. 20-41.

[21] The legal measures adopted distinguish, either directly or indirectly, between the main types of cells and stem cells, such as adult cells, blood stem cells, totipotent and pluripotent stem cells, but they very rarely engage closer with stem cell technology, for instance by distinguishing between hESC and iPSC, and tend to keep their prohibitions and permissions at a more general regulatory level.

or iPSC.[22] The majority of them focus on the protection of human embryonic life, addressing that issue in the general context of biomedical research and/or human assisted reproduction.[23] Only some put particular emphasis on regulating in detail the corresponding institutional and procedural environment. Even though the foundations, such as the commitment to protect the value of human (embryonic) life and of human biological material and the dedication to safeguard human integrity and autonomy (and self-determination) are similar and shared, expressing local difference is a particularly important frame of regulation.[24] As demonstrated below, the local context has had considerable influence on the detailed regulation of generic regulatory issues, such as informed consent, the information rights provided to individuals, the prohibition of financial gain, the prohibition of commercially-oriented conduct, the requirement of purpose-bound and proportionate human intervention, and the requirement to adhere to scientific standards in biomedical research.

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22 Germany: the Stem Cell Act (on pluripotent human stem cells) and the Transfusions Act (on blood stem cells). See also the Dutch Embryo Act's limited hESC-related provisions, and the provisions of the French Public Health Code and of the Belgian Act on the Procurement and Use of Human Bodily Material on hESC. The applicable Canadian measure, the CIHR Updated Guidelines for Human Pluripotent Stem Cell Research (2010), integrated into the 2nd Edition of the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans, distinguishes between hESC, iPSC and human embryonic germ cell (hEGC) lines and other pluripotent stem cell lines.

23 Separate laws for the protection of human embryos were adopted in Belgium, Germany, and the Netherlands. This does not mean that human embryonic life would not be protected in more general legal measures in other countries. France represents a specific case as all relevant rules on medicine and biomedical research are regulated in the general Public Health Code, which has specific provisions on human embryos and hESC on human assisted reproduction and supernumerary embryos, and on the procurement and the donation of human biological material. The Hungarian Act on the Protection of Human Embryonic life (Act 1992:LXXIX) focuses solely on in vivo embryos and foetuses, and regulates the termination of pregnancies.

24 This is most visible in the regulation of permitted sources of stem cells. There are restrictive regimes, such as Austria or Germany which strictly limit potential sources of stem cells, medium regimes, such as Hungary, the Netherlands, or France which exclude certain, ethically controversial sources of stem cells based on value-based considerations, or liberal regimes such as the UK or Belgium which recognise a broader spectrum of legitimate sources of stem cells. Other, more detailed (and issue specific) classifications are also available, see *Human Stem Cell Research and Regenerative Medicine* (Strasbourg: European Science Foundation, 2013).

The introduction of stem cell-specific instruments, when that was considered necessary, and the alternative of introducing stem cell-specific rules into generic measures seem to have followed different objectives in the different states. Protecting – mainly in vitro – human (embryonic) life serves as the main regulatory objective in most states, either explicitly (for example, Austria, Germany, Belgium and the Netherlands),[25] or implicitly (the UK and Hungary).[26] Advancing healthcare and biomedical research are presented as parallel objectives in a number of countries.[27] Regulating stem cells and their application appeared as a specific objective in a few states (for example, Germany, Belgium and France).[28] The regulation of stem cell technologies, stem cell procurement in particular, as a part of comprehensive codes governing health care and biomedical research, as in the case of France, necessarily means that regulatory intervention is subject to multiple and overlapping objectives with specific objectives influencing the regulation of particular domains within the code. For example, the protection of persons involved in donation, regulation of tissue and

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25 And the protection of the woman involved (Germany, the Embryo Protection Act). The Belgian rules have a strong focus on the regulation of the fate of supernumerary embryos created in a parental project. The Dutch Embryo Act also contains extensive provisions on biomedical research using human embryos. The Netherlands has a separate act for the protection of human foetal life (the life of the human fruit) and for the procurement of human foetal tissue. The Austrian Act on Medically Assisted Reproduction regulates this issue predominantly in the general technological context of human (assisted) reproduction.

26 The UK: Human Fertilisation and Embryology Act 1990. Hungary: Act on Health Care.

27 For example, Belgium, Germany and the Netherlands.

28 The Belgian Act on the Procurement and Use of Human Bodily Material defines stem cells as cells of human origin capable of self-renewal and differentiation to one or multiple specialist human cells. The German regulatory framework relies on a distinction between totipotent and pluripotent (stem) cells when defining the human embryo and regulating stem cells. The Stem Cell Act defines pluripotent cells as all human cells which have the capacity for development through cell division and which can develop into different specialised cells, which, however, are unable to develop into a human being. hESC are defined as pluripotent cells harvested in vitro from a supernumerary human embryo. It also gives a definition to hESC lines as hESC which are maintained in a cell culture or stored in a cryoconserved state. The Transfusions Act defines blood stem cells.

cell procurement, or availability of human embryos for reproductive or for biomedical research purposes.[29]

The differences between national regimes regulating matters that are directly relevant for stem cell procurement are most striking when the definitions provided in law for the human embryo are considered. These differences seem to have an impact on the particular orientation and overall character of national regulation.[30] The local definitions range from extremely broad to precise and detailed. Austrian law introduced the rather broad concept of "viable cells" which gave way to a prohibitive, and not particularly effective, national regulatory framework.[31] German law provides a detailed regulation of the embryo and its potentiality as a fertilised and viable[32] human egg, also including totipotent cells removed from a human embryo,[33] which – together with the

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29 Which may include other overarching objectives, such as the protection of the rights and the dignity of persons in health care (see the French Public Health Code, arts. L1110-1 – L1110-3).

30 See also the national particular regulatory concept of "*Individuum*" in Germany, the explicit German intention to protect embryos *and* women, or the focus of the French Public Health Code on the different groups of persons requiring special legal protection.

31 "entwicklungsfähigen Zellen", which covers fertilised egg cells and cells developed from them (Act on Medically Assisted Reproduction, art. 9(1)). It is unclear what "cells developed from them" stands for, especially whether it covers pluripotent stem cells, hESC in particular, procured in Austria or abroad, and whether it, thus, prevents their use for purposes other than assisted human reproduction. Since the concept does not distinguish between totipotent and pluripotent stem cells and does not recognise sources for "viable cells" other than the human body, it is unclear what legal status is available for iPSC in Austria. According to commentators, the breadth of the concept of "viable cells" indicates that the prohibition included in art. 9(1) goes beyond the aim of protecting human embryos and has the effect of preventing hESC and iPSC research in Austria, see Christian Kopetzki, "Zur Lage der embryonale Stammzellen in Österreich" in Hans-Jürgen Ahrens, Christian von Bahr, Gerfried Fischer, Andreas Spickhoff and Jochen Taupitz (eds.), *Medizin und Haftung* (Berlin: Springer, 2009) 297-315.

32 Viability is also defined in the Embryo Protection Act: the fertilised human egg must be regarded as viable in the first 24 hours after the fusion of the nucleus, except when it is established that it is unable to develop beyond the single cell stage.

33 In the Stem Cell Act, it is defined as every human totipotent cell. The Medicines Act states that human gametes, fertilised human eggs and human embryos are neither medicines nor tissue preparations.

exacting regulatory definition of pluripotent[34] stem cells, hESC in particular[35] – provides the foundation of a meticulously regulated, restrictive framework for hESC research.[36] In the UK, the embryo is defined as a living human embryo where fertilisation is completed (after the appearance of the two cell zygote), which includes an egg in the process of fertilisation or undergoing any other processes capable of resulting in an embryo,[37] which serves as the basis of the broad range of activities permitted in legislation. Also, there are regimes which lack a purpose-made definition (France),[38] or which use only a general concept without any specific regulatory consequences associated in the stem cell domain (Hungary),[39] which, however, does not seem to affect the scope and depth of regulation. The regimes in the Netherlands and Belgium focus on defining potentiality (embryo which is a cell or collection of cells which is capable of developing into a human being), which definitions underpin the sophisticated rule-based frameworks in place concerning the use of human embryos.[40]

3.1 Protecting rights and values

In Europe, the incorporation of the relevant bioethical considerations into biomedical technology regulation – often rather explicitly and through restrictive

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34 Potentiality refers to the ability of different cells to differentiate into different cell types. Curiously, potentiality and the distinction between different forms of potentiality, as a matter of producing clear and precise legal definitions, did not receive much attention in Europe neither at the national, nor at the European level.

35 *Supra* n. 28.

36 The Embryo Protection Act and the Stem Cell Act.

37 Human Fertilisation and Embryology Act 1990.

38 The definition applicable in law is that provided in art. 16-1 of the Civil Code which "guarantees the respect of every human being from the beginning of its life".

39 Act on Health Care. As an indication of achievable levels of regulatory detail, the Hungarian regime also regulates the fate of "unlawfully donated", "refused" and "damaged" human embryos.

40 In Belgium, in three separate measures regulating the procurement and use of human bodily material, regulating assisted human reproduction and regulating research on in vitro human embryos. In the Netherlands, in the Embryo Act.

or prohibitive rules – is one of the dominant[41] regulatory frames.[42] This is particularly visible in the central regulatory distinctions used in legislation and also in the corresponding lists of restricted and prohibited activities (Table 2). As also indicated earlier, the main value regulated in the different national measures governing reproductive medicine and embryology is the protection of the value of human (embryonic) life and human biological material (for example, human cells, gametes and tissues). The right to respect for the integrity and autonomy of individual human beings is also part of the regulatory framework. These values and rights then give rise to balancing exercises in the application of the provisions in question between the private and public interests at stake (for example, between the interests of biomedical research and the rights and interests of individuals).[43] The outcome of these balancing exercises is largely affected by the aforementioned, ethically influenced, regulatory distinctions and categorisations made in the different measures.

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41 As it follows from the Oviedo Convention on Human Rights and Biomedicine (ETS No. 164). The Oviedo Convention includes rights and values, such as putting human dignity and integrity at the centre of biomedical regulation, balancing the interests and welfare of human beings against the interests of science, protecting the autonomy of the person through the informed consent rule, protecting privacy and confidentiality, protecting the integrity of the human genome, the protection of human embryos in research, protecting tissue and organ donors, prohibiting financial gain, or the prohibition of the use of human embryos for research purposes. See also the stem cell-relevant jurisprudence developed under the European Convention on Human Rights, such as *Durisotto*, *supra* n. 9, which rejected the violation of the right to private life by the refusal of access to an experimental stem cell therapy, the therapeutic value of which had not been established, and *Parillo v Italy*, Judgment of 27 August 2015, App. No. 46470/11, nyr. (ECtHR), which rejected the violation of the right to private life by the refusal to allow a woman to donate in vitro embryos for research purposes when that was not permitted by national law adopted to strike a balance between the relevant rights and interests.

42 These could change over time as indicated by the 2013 modification of art. L2151-5 of the French Public Health Code by Act 2013-715 of 6 August 2013 which changed the original general rule prohibiting – subject to exceptions – research on human embryos, hESC and hESC lines to a general rule which permits research on human embryos and hESC provided that it has been duly authorised.

43 The Oviedo Convention provides the common basis in Europe for such balancing exercises. See arts. 15 and 16 on the requirement of balancing between the risks and the benefits, the obligation to seek for alternative solutions, and the benchmark of ensuring the justifiability and the necessity of the intervention, which provisions also form part of the ethics- and human rights-based frame of technology regulation.

The most pertinent regulatory distinctions concern the use of human biological material, including human embryos,[44] and involve distinctions: between uses in a parental project (in an assisted reproduction process) and other purposes, such as biomedical research or therapy, or education;[45] between permitted (authorised/licensed) and prohibited (non-authorised/non-licensed) uses; and between primary and secondary uses of human biological material.[46] A similarly crucial distinction is that made between in vitro and in vivo interventions and between in vitro and in vivo human biological material, especially between in vitro and in vivo human embryos. The distinctions between living and deceased persons in donation, and between adults, minors, and persons under legal guardianship, representing different states of personhood, also have significant ethical relevance. The restrictive German regime operating an exception for imported hESC includes the ethically controversial distinction between activities involving hESC in Germany and abroad, and between domestic and imported hESC.[47] There are further important regulatory distinctions which determine the overall ethical integrity of national frameworks. These include the distinctions between activities for the benefit of the individuals (donor) concerned and other activities, between necessary and unnecessary interventions, between scientifically and professionally sound and unsound interventions, and between research conducted following legitimate and illegitimate research aims. A few countries (Hungary and the Netherlands)

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44 In Germany, also hESC (Stem Cell Act).

45 See the general distinction in Germany between the legitimate uses and misuses of biomedicine (Embryo Protection Act).

46 The distinction in the Austrian Act on Medically Assisted Reproduction between uses of gametes and "viable cells" in assisted reproduction and for other purposes is responsible for the implied prohibition on the procurement of hESC from "viable cells". It may also exclude the manipulation of the cells covered, especially the creation of embryos for research purposes through cloning. See Kopetzki, "Zur Lage", *supra* n. 31.

47 The UK also distinguishes between UK and imported human biological material.

regulate explicit distinctions between invasive and non-invasive interventions and between the intentional and non-intentional changing of the conditions of the research subject.

Table 2. The relevant restricted and prohibited activities in national measures.

Austria					
Purpose-bound procurement (of gametes and gonad tissues) (for a parental project).	Restriction, on the basis of a requirement of necessity, of the number of embryos (fertilised oocytes) created in a parental project.	Restricted, purpose-bound use of oocytes, viable cells and gametes (for a parental project) (to the benefit of the person involved).	Intervention with the germ line (prohibited).		
Belgium					
Purpose-bound procurement (of human bodily	Purpose-bound use (of human bodily material)	Purpose-bound use of supernumerary human embryos	Purpose-bound use of supernumerary	Creating human embryos for research	Commercialisation (the commercial use) of (supernumerary)

material) (for human use and therapy).	(for prevention, diagnosis, therapy and research).	(for the purpose of advancing human knowledge in health care).	human embryos (only for the purpose specified in advance in an agreement between the persons concerned).	purposes (prohibited with an exception).	human embryos, gametes and hESC (prohibited).
Reproductive human cloning (prohibited).	Creating hybrids and chimeras (prohibited).	Implanting research embryos into humans (prohibited with an exception).			
France					

Purpose-bound use (of parts and products of the human body) (for medical or scientific research purposes).	Purpose-bound use (of parts and products of the human body) (the uses must be determined in advance at the time of procurement and other uses must be communicated to the persons concerned).	Procuring tissues and cells from minors or adult persons under legal guardianship (prohibited with strictly regulated exceptions).	Procurement (conservation and use) of embryonic and foetal tissues and cells in the context of the termination of a pregnancy from a woman, who is either a minor or an adult under legal guardianship (prohibited with an exception).	Transfer for reproduction purposes of research embryos (prohibited).	Creating and using human embryos for commercial or industrial purposes (prohibited).

Restriction, on the basis of a requirement of strict necessity, of the number of embryos (fertilised oocytes) created in a parental project.	Human reproductive cloning (prohibited) (Article 16-4, Code Civil).	Human cloning (the creation of human embryos) for research or therapeutic purposes (prohibited).	Creating human embryos by in vitro fertilisation for research purposes (prohibited).	Creating transgenic or chimeric embryos (prohibited).	Creating embryos in a parental project and their donation for research (permitted subject to conditions).
Procurement of tissues and cells (general) (permitted subject to conditions).	Procurement of hematopoietic cells from cord blood and the placenta (and cells from the umbilical	Procurement, conservation and use of embryonic and foetal tissues and cells in the context of the	Donation and use of gametes (permitted subject to conditions).	Research on human embryos and hES cells (permitted subject to conditions).	

	cord and the placenta) (permitted subject to conditions).	termination of pregnancy (permitted subject to conditions).			
Germany					
Purpose-bound fertilisation of the egg/placing of the sperm cell into the egg (for the purpose of a parental project).	Restriction, on the basis of a requirement of necessity, of the number of embryos (fertilised oocytes) created in a parental project.	Creating in vitro human embryos for purposes other than being used in a parental project (prohibited).	Purpose-bound use of in vitro human embryos.	Selling in vitro embryos or embryos removed from the uterus before nidation (prohibited).	Releasing, purchasing or using human embryos for purposes that do not serve their preservation (prohibited).

Trading donated organs and tissues (prohibited).	Changing the human germ line (with exceptions) (prohibited).	Creating chimeras and hybrids (prohibited).	Human cloning for any purposes (prohibited).	Import and uses of hESC, with the exception of importing hESC for research purposes and their subsequent use in research (prohibited).	
Purpose-bound procurement and use of tissues and cells (for therapeutic purposes)	Procurement of tissues and cells (general) (permitted subject to conditions).	Procurement of tissues and cells from deceased embryos and foetuses (permitted subject to conditions).	Use of blood stem cells (permitted subject to conditions).		
Hungary					

Purpose-bound donation of gametes and embryos (for parental project or biomedical research).	Purpose-bound use of gametes (for the purposes specified at the time of donation).	Creating human embryos for research purposes (prohibited).	Implanting a human embryo into an animal (prohibited).	Fertilisation of human and animal gametes (prohibited).	Using human embryos for the creation of multiple embryos or for the creation of human beings with characteristics unavailable through fertilisation (prohibited).
Donating gametes (permitted subject to conditions).	Donating in vitro human embryos (for parental project or for	Procurement of bone marrow, hematopoietic stem cells and	Human cloning (reproductive and research) (prohibited).	Modifying the genome of the human offspring (prohibited).	

	biomedical research (permitted subject to conditions).	other regenerative tissue (permitted subject to conditions).			
The Netherlands					
Purpose bound creation and use of human embryos.	Donating gametes (for parental project or research) (permitted subject to conditions).	Donating in vitro embryos (for parental project or research) (permitted subject to conditions).	Donating gametes for the creation of in vitro embryos (permitted subject to conditions).	Commercialisation (the offering of gametes and embryos for use for permitted purposes at a price higher than the cost of procuring and storing them)(prohibited).	Modifying germ line genetic identity (prohibited).

Using gametes and embryos for purposes other than those specified in legislation (prohibited).	Using cells procured from embryos for purposes other than those specified in legislation (prohibited).	Reproductive human cloning (prohibited).	Allowing the development of in vitro embryos beyond 2 weeks (prohibited).	Intentional modification of genetic material in the nucleus of gametes made available in a parental project (prohibited).	Creating hybrids and chimeras (prohibited).
Keeping of germ cells and other parts derived from a human foetus for the purposes of human reproduction or for other non-	Using cells derived from foetal tissue for other than the permitted purposes (prohibited).	Removing parts from a living born human fruit based on the prospective intended uses of foetal tissues (prohibited).	Using foetal tissue for the medical treatment of persons designated by the woman (prohibited).		

therapeutic purposes (prohibited).					
United Kingdom					
Creating, keeping and using (and procuring and distributing) in vitro human embryos (permitted subject to a license).	Creating, keeping and using in vitro human admixed embryos (permitted subject to a license).	Keeping or using gametes and embryos in circumstances in which regulations prohibit their keeping and use (prohibited).	Keeping and using of an embryo (and a human admixed embryo) after the appearance of the primitive streak (prohibited).	Altering the genetic structure of any cell while it forms part of a human embryo (prohibited).	Replacing a nucleus of a cell of an embryo with a nucleus taken from a cell of any person, embryo, or subsequent development of an embryo (prohibited).

The reliance on supernumerary human embryos as a source of hESC led in most regulatory regimes to targeted responses to the controversies raised by this technological development. The focus is on regulating their availability for the procurement of stem cells. The law in Belgium and in the Netherlands accepts their availability explicitly.[48] The Austrian and German regimes, formulating their prohibitions indirectly, exclude supernumerary embryos as sources of stem cells.[49] Other states address this issue in the context of regulating the fate of unused in vitro embryos created in a parental project. French law, having recognised the need to provide strong legal protection to them, introduced a detailed regulation of the legal safeguards applicable in the relevant procedures, which rules read together make it clear that procurement from donated supernumerary embryos is the only lawful source of hESC.[50] Hungarian law regulates a right of disposal over supernumerary embryos and the legal assumption that in case the right of disposal has not been exercised they should be put into deposit for further use.[51] The UK secures their availability by defining specifically the legal category of in vitro embryos.[52]

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48 In Belgium, their availability, donation, storage and use as regulated in the Act on Medically Assisted Reproduction and on the Fate of Supernumerary Embryos and Gametes. The act, and the Act on Research on In Vitro Human Embryos, gives a specific definition for supernumerary embryos as human embryos created in a parental project which were not implanted into the female womb. It also defines supernumerary gametes as gametes which were procured in a parental project but were not used (the act distinguishes between gamete providers and donors, the former referring to a person from whom gametes are procured for research purposes and the latter to a person who donates gametes for a parental project). The Dutch Embryo Act mentions the procuring of hESC as one of the legitimate objectives of embryo donation.

49 German law applies a distinction between human embryos and pluripotent stem cells, and prohibits the use of human embryos for research purposes under German jurisdiction. The Austrian concept of "viable cells", because of its general scope and its failure to distinguish between the different stages and forms of human embryonic development, provides a controversial legal basis for the prohibitive regime established (*supra* n. 31, 46). Austrian law also lacks the concept "supernumerary embryos" which, read in light of the relevant strict legislative provisions, further supports the conclusion that under law human embryos are not available as sources of stem cells. The legal status of imported stem cells, including hESC – Austrian law lacking provisions for this purpose – is less certain, and they may be available for research.

50 Public Health Code, art. L2151-5.

51 Act on Health Care, ch. 9.

52 Human Fertilisation and Embryology Act 1990, sch. 2.

Where the use of supernumerary embryos for research purposes is permitted, national regulation resorts to the following means of introducing ethics-based boundaries for conduct. Belgian law uses a legal distinction between human embryos and foetuses at eight weeks of embryonic development, which needs to be interpreted together with the rule which prohibits research on embryos after the fourteenth day of their development.[53] UK law recognises a similar rule which prohibits the keeping or using of an embryo after the appearance of the primitive streak (not later than the end of the period of fourteen days beginning with the day when the gametes are mixed, not counting any time during which the embryo is stored).[54] Hungary applies a twelve-week rule to separate embryos and foetuses, which needs to be applied together with the provision which allows research embryos to be kept alive for fourteen days.[55] The law in the Netherlands relies on a distinction between human embryos, foetuses and "human fruit", which needs to be read together with the prohibition on allowing the development of in vitro embryos beyond two weeks.[56]

The national measures contain further, predominantly ethics-based[57] components relevant for stem cell procurement. While the principles regulated are shared among the different states, their regulation applies different standards, legal safeguards and institutional-procedural arrangements, which differences indicate that connections with the technology were defined having regard to local considerations. The prohibition on financial gain is recognised in every national regime investigated. They are, however, far from uniform in regulating the costs available for reimbursement in the special context of cell and

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53 Act on the Procurement and Use of Human Bodily Material, art. 2 and Act on Research on In Vitro Human Embryos, art. 3(5).
54 Human Fertilisation and Embryology Act 1990, art. 3(4).
55 Act on Health Care, arts. 165, 181.
56 The Embryo Act, art. 1 and the Foetal Tissue Act, art. 1.
57 The balancing of conflicting interests, the regulation of technological possibilities and scientific appropriateness are other factors addressed in these rules.

tissue donation and procurement.[58] Similarly, while the principle of informed consent is recognised in the different national laws, its details, for instance the actual scope of the consent given or the formalities of providing consent, are regulated differently.[59] The most notable of these are the French provisions which in certain circumstances apply specific procedural and institutional, and sometimes substantive limitations.[60] Hungarian law also subjects giving and obtaining informed consent to specific formal and substantive conditions in particular situations.[61] A further shared requirement is that interventions, including the procurement of hESC, must be scientifically justifiable, conform to scientific standards, or be subject to scientific supervision.[62] Some states adopted a particularly detailed regulation of this requirement.[63] As a general benchmark, the regulatory systems investigated, although in different ways, require that human conduct in the biomedical research context must be proportionate and necessary.[64] The French regime provides an important locally specific example for the regulation of legally secured information rights of individuals and the parallel information obligations of the relevant institutional actors.[65]

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58 Austria: Act on Medically Assisted Reproduction, art. 16; Belgium: Act on the Procurement and Use of Human Bodily Material, art. 6 and Act on Medically Assisted Reproduction, art. 48; France: Public Health Code, arts. L1211-4, L1244-7; Germany: Stem Cell Act, art. 4 and Transplantations Act, art. 2; Hungary: Act on Health Care, art. 170; the Netherlands: Act on the Quality and Safety of Bodily Material, art. 3a.

59 Austria: Act on Medically Assisted Reproduction, art. 8; Belgium: Act on the Procurement and Use of Human Bodily Material, art. 10, Act on Research on In Vitro Embryos, art. 8 and Act on Medically Assisted Reproduction arts. 12 and 41; Germany: Embryo Protection Act, art. 4 and Transplantations Act, art. 3; the Netherlands: Embryo Act, art. 5 and Foetal Tissue Act, art. 6; the UK: Human Fertilisation and Embryology Act 1990, sch. 3.

60 Public Health Code, arts. L1211-2, L1221-5 and L1231-1.

61 Act on Health Care, arts. 159, 176.

62 Belgium: Act on Research on In Vitro Embryos, art. 3; France: Public Health Code, art. L2151-5; Germany: Embryo Protection Act, art. 4; the Netherlands: Embryo Act, art. 2.

63 Act on Health Care, art. 159.

64 Belgium: Act on Research on In Vitro Embryos, arts. 3, 4 and Act on the Procurement and Use of Human Bodily Material, art. 10; France: Public Health Code, art. L-1211-6; Germany: Embryo Protection Act, art. 4 and Transplantations Act, art. 8; Hungary: Act on Health Care, art. 164; the Netherlands: Embryo Act, art. 3; the UK: Human Fertilisation and Embryology Act 1990, sch. 2.

65 Public Health Code, arts. L1211-2, L1244-7, L2141-4, L2151-1. See also in Germany Transplantations Act, art. 7.

There are other country-specific value-influenced restrictions in different areas of regulation, which may affect – as parts of the general regulatory framework – the availability of certain source-materials for stem cell procurement. As seen in Table 2, most national regimes include restrictions on the number of embryos created in a parental project, which rely, in one form or another, on a test of necessity. In connection with the earlier mentioned right of disposal over supernumerary embryos, Hungarian law recognises the possibility of refusing the donation of embryos in cases when their use for the declared purpose within the time available is unlikely and when it is likely that a human being will develop from the embryo.[66] "Refused" embryos as well as unlawfully donated and damaged embryos are subject to provisions regulating their handing over to the responsible institution, and there are rules on the responsibility of the holders of embryos for their storage or destruction in case they are not taken by that institution.[67] Austrian law bans the mediation ("*Vermittlung*") of viable cells and gametes and of persons capable of providing viable cells and gametes for a parental project.[68] The commercial advertising of the donation and the mediation of viable cells and gametes in the context of assisted human reproduction processes is also prohibited.[69] Belgian law also contains an explicit ban on publicising, except when it is the interest of public health protection, the donation of human bodily material.[70] French law includes a prohibition on receiving remuneration for activities associated with tissue and cell procurement.[71] Hungary also applies a prohibition on providing or asking

66 Act on Health Care, art. 176.
67 *Ibid*.
68 Act on Medically Assisted Reproduction, art. 16.
69 *Ibid*.
70 Act on the Procurement and Use of Human Bodily Material, art. 5.
71 Public Health Code, art. L1211-4.

for remuneration in the donation of human gametes.[72] The Hungarian act governing the obligation of the state to recover justified damages in the context of tissue and cell procurement and the clause declaring the liability of the state for damages or death caused in the context of authorised biomedical research provide crucial supportive components of the domestic regulatory environment.[73] Further examples of supportive national regulation include the French provisions regulating the statutory leave available for donor examination, ovarian stimulation and for oocyte procurement in the context of gamete procurement, the specific obligation to reimburse oocyte donors for the expenses incurred with the donation, and the specific rules about protecting the interests of the persons involved.[74]

3.2 Risk, quality and safety

The national measures governing tissue and cell procurement, partly as a consequence of the implementation of the EU Tissues and Cells Directive,[75] are characterised by a detailed framework for regulating risk, quality and safety. Generally, they focus on the conditions of tissue donation and procurement, on the rights of donors including informed consent, and on the obligations of institutional actors in the processing, storing, transportation and in the related administration of donated material. The risk, quality and safety rules in the different Member States are, however, by no means uniform. This is indicated foremost by the uneven practices of implementing the EU directive. There are national measures which achieved implementation without notable

72 Act on Health Care, art. 173(3).
73 Act on Health Care, art. 164.
74 Public Health Code, arts. L1244-5.
75 *Supra* n. 20.

modifications (for example, Austria and the Netherlands).[76] There are others which implemented the directive with some structural adjustments so as to ensure that its requirements are duly integrated into existing national regulatory frameworks (for example, France and Germany).[77] Finally, there are regimes which incorporated EU rules with both structural and substantive adjustments made to national law (for example, the UK and Belgium).[78] These differences in the implementation strategy followed by individual Member States suggest considerable divergences regarding the relevance in national law and policy of the domain regulated, and the approaches pursued in the application and enforcement of the rules in question.[79]

3.3 Institutionalisation and proceduralisation

The national regulatory systems examined all operate an institutional framework for the ethical and other expert (for example, biomedical or technological) supervision of stem cell related activities, including stem cell procurement, and they provide for regulated procedures governing particular aspects of those activities, such as securing research authorisation or obtaining informed consent. Again, in part, this is the outcome of the implementation of the relevant EU obligations which, in regulating risk, and quality and safety, place considerable emphasis on putting in place effective institutions and procedures.[80] The national institutional and procedural settings, however, exhibit considerable variety as to

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76 See Act on Tissue Quality and Safety in Austria and Act on the Quality and Safety of Body Materials in the Netherlands.

77 France: Public Health Code, Book 2. Germany: Transplantations Act.

78 See Act on the Procurement and Use of Human Bodily Material in Belgium and Human Tissue Act 2004 in the UK.

79 See A Mahalatchimy et al, "The Legal Landscape for Advanced Therapies: Material and Institutional Implementation of European Union Rules in France and the United Kingdom" (2012) 9 *Journal of Law and Society* 131-149.

80 See the EU Tissues and Cells Directive, arts. 16-28.

the bodies established, the powers granted to those bodies, the allocation of responsibilities, the design of institutional rules, the regulation of the standards of conduct, the protection of the rights and interests of the individuals concerned, and in regards how institutional communication and information flow are organised.[81] Among the bodies established in the different regimes, we find national (and other) medicines agencies, ethical councils, biomedical research bodies, central registries, and other "responsible authorities". The national procedural rules, which aim to ensure that the powers available to the institutions, including enforcement and sanctioning powers, are exercised in an ordered fashion, subject to requirements of transparency and accessibility, and with due regard to the rights and interests of the parties, also reveal genuine differences as to the level of their detail and sophistication.[82]

3.4 Local diversity

Expressing local diversity in the regulation stem cell technologies provides an inevitable theme for national regulation.[83] As bound by higher legal norms, or affected by judicial interpretation, national measures often express – in legal prohibitions or in legally prescribed balancing exercise between competing values or interests – genuinely local considerations. Austria serves as a curious example in this regard because the comparatively narrow scope of protection

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[81] See, for example, the particular Dutch approach of framing the relevant prohibitions and permissions as institutional and procedural rules in the Embryo Act. See also *supra* n. 65 on the particular national examples for regulating information rights and the corresponding institutional obligations.

[82] See the specific provisions in France on obtaining informed consent, the Dutch rules on obtaining an authorisation for the "research protocol", or the German approach of regulating the conditions of decision-making in the national institutional and procedural framework.

[83] For the EU level, this appears as the obligation to respect and accommodate local diversity, for example under the Tissues and Cells Directive, art. 4(3) recognises local discretion in deciding which specific type of human cells, especially which germ cells and embryonic stem cells may be used and which will be excluded from being used for human application.

offered under the rather generally elaborated constitutional standard[84] is not matched by the interpretations available to the applicable legislative text.[85] In contrast to the Austrian example, the deference of the Belgian constitutional court to the legislature in questions of biomedical ethics can be seen as having played a role in Belgium adopting an overall permissive and supportive regulatory framework.[86] Similarly, the provisions of the French Public Health Code seem to be in harmony with the approach of the Constitutional Council which deferred on matters of morality and policy in biomedicine to the discretion of the legislator, demanding nevertheless that an adequate balance is established between the competing rights and values laid down in the constitution.[87] In Hungary, the deference allowed under the Constitution has been used by the legislator to establish and maintain a relatively permissive regime for stem cell technologies, at least as far as hESC are concerned.[88] Conversely, the German constitutional court's uncompromising position on the right to life and human dignity seems to have found expression in the restrictive German measures.[89] In the UK, the particular features of the Human Fertilisation and Embryology Act 1990 do not follow from higher-ranking legal principles, rather from the outcomes of a broad and ambitious social discourse.[90] Notice must be taken, however, of the ruling in *Quintavalle*,[91] which produced a flexible legal understanding of the original legislative intent behind the act, which measure was then interpreted to cover technological developments that occurred

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84 Decision of the Austrian Constitutional Court: VfSlg. 7400/1974 (Fristenlösung) on abortion.

85 *Supra* n. 31, 46, 49.

86 Decisions of the Belgian Constitutional Court 39/1991 and 146/2011.

87 Decisions of the Constitutional Council 94-343/944 DC, 2001/446 and 647/2013.

88 Decisions of the Constitutional Court 23/1990 (Capital punishment), 64/1991 (Abortion), and 48/1988 (Abortion).

89 Decisions of the Constitutional Court BvF 2/90, 2 BvF 4/92 and 2 BvF 5/92.

90 See the *Report of the Committee of Inquiry into Human Fertilisation and Embryology* (the Warnock report) (London: UK Department of Health and Social Security, 1984).

91 *Quintavalle v Human Fertilisation and Embryology Authority* [2005] UKHL 28.

subsequent to its introduction.

4 Specific or generic? Analysing frames of stem cell procurement regulation

The national regulatory frameworks for stem cell procurement examined above, as reflected in the regulatory frames applied and their expression in legal rules, are essentially mixed regimes combining, although in a variety of ways, generic and stem cell technology-specific provisions. The different national regimes, although they operate with comparable rules serving similar objectives and find connection using technology-specific provisions with the technology regulated generally in a similar manner, are characterised by different approaches concerning the focal points of regulation, the details of the rules provided, and concerning the choice between generic and technology-specific provisions. Even though they tend to regulate stem cell technologies by way of introducing prohibitions and conditional permissions,[92] by securing individual rights and imposing institutional obligations, and by means of providing for an institutional and procedural framework, the national systems exhibit crucial differences in developing bio-legal categorisations and concepts, and in making with the help of these the connection with the technology regulated. As discussed above, they differentiate between the different stem cell technologies, regulate the different sources of stem cell procurement, and govern the broader biomedical context of stem cell procurement in distinct ways.

Regulatory unevenness was clearly an issue in most of the national regimes. On the one hand, there were issues which received prioritised

[92] On the generally prohibitive nature of regulation concerning the procurement of human biological material and on the reluctance to lift the restrictions on such activities, see Hoppe, *Bioequity*, *supra* n. 14.

regulatory attention (for example, the donation of supernumerary embryos). On the other, some issues which have similar importance from the perspective of the general objectives of regulatory intervention continue to suffer from under-regulation (for example, the non-commercialisation principle). Some of this unevenness is, necessarily, the result of uncertainty as to the future application of rules in a new technological context which can justify caution when introducing detailed rules. For example, it is uncertain how in the context of the procurement of hESC lines the restriction concerning the separation of the cells of the human embryo, introduced originally in a preimplantation genetic diagnosis context, will play out.

From the perspective of the core question of this article whether generic or technology-specific measures should be preferred in securing connection between regulation and the technology regulated, the variety exhibited in the earlier comparative overview made it clear that it would be difficult to identify a single best regulatory approach or regulatory solution. The national regimes all have better developed and less sophisticated components,[93] and considering that the general regulatory framework governing biomedicine and biomedical research plays a crucial role, the possibility of regulatory improvement is not limited to the stem cell technology-specific provisions. As a matter of the choice between generic and technology-specific provisions, this mixity of national regimes and their respective variety offer two major conclusions. On the one hand, many of the issues of stem cell procurement, and of stem cell technologies themselves, are not specific to the technology which would then require targeted regulatory intervention. On the other, from the perspective of the technology in question, well-defined and well-operated generic measures governing the

[93] See the different range and variety of prohibitions and restrictions in the different national regimes as compiled in Table 2.

broader environment are just as important as adequately targeted technology-specific provisions. Connecting regulation with stem cell technologies, stem cell procurement in particular, requires not only a clear delimitation between the permitted and prohibited sources of stem cells, but also a sound regulation of safeguards in the relevant decision-making procedures, or of the information rights of individuals and the corresponding information obligations of the relevant institutional actors. There is, thus, a broad scope for improving national regulatory mixes by way of learning from other regimes and considering the borrowing of both generic and technology-specific provisions from them.

The current state of regulating stem cell procurement technologies in the different European countries as discussed here seems to correspond with what follows from the pitfalls and dilemmas of regulating emerging biotechnologies mentioned earlier.[94] The focus on regulating human embryology and the fate and uses of supernumerary embryos in a domain that is much broader than the procurement and the use of hESC can be regarded as suggesting uncertainties in the law, approaching an evolving technology with its categorisations and with its desire to subject the technology to law's formalised treatment. The complexities of establishing and maintaining regulatory connection that is effective, efficient, legitimate and democratic, achieving which, in the absence of definitive solutions, supports the need for cross-border regulatory learning and borrowing, were also made evident.[95] The national regimes examined do not seem to have secured the balance between these qualities of technology regulation. For instance, while the German regime contains a convincing

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[94] *Supra* n. 10-14.

[95] The Canadian regime offers an interesting example. It combines hard legislation and soft governance. The detailed stem cell technology-specific rules are laid down in the non-binding soft instrument (the CIHR Guidelines), which rules, nonetheless, find their basis in the fundamental prohibitions laid down in legislation, the Assisted Human Reproduction Act. This solution seems to provide flexibility to regulation and it also pays attention to the demands of stakeholder compliance.

framework of detailed and sophisticated rules governing the stem cell procurement domain with clear prohibitions and sanctions which give expression to the moral hazards of stem cell technologies, the exception included concerning the use of imported hESC in German territory suggests that the burdens, thus imposed on local stakeholders, were considered to be far from ideal from the perspective of the practical objectives pursued in biomedicine and biomedical research. As another example, although the direct regulation of hESC procurement and technologies, as pursued by France and Belgium, may be considered as being capable of securing regulatory effectiveness, new technological developments, such as the emergence of iPSC, may render the rules thus enacted obsolete and inefficient. The example of Austria shows, however, that the alternative of relying on general regulatory categories may not offer a satisfactory solution. The underpinning of the prohibitive regulatory framework in Austria with the rather opaque concept of "viable cells" led to considerable uncertainties as to the scope of the applicable prohibitions, which uncertainties put the effectiveness of regulation in jeopardy.

The earlier comparison of national regimes also highlighted that, as a matter of the complications of connecting rules with the technology regulated, there is a fundamental difference between prohibitive and permissive regimes of stem cell procurement regulation.[96] Prohibitive regimes have an easier task in achieving their objectives by means of legal regulation. They can rely on the instruments familiar to law, such as the introduction of legally sanctioned prohibitions, when delineating prohibited from the far less numerous permitted conducts. This is not to say, however, that prohibitive regimes are without fault

[96] See the classification introduced in *supra* n. 24.

and that they are similarly effective in securing their aims.[97] For example, while the German framework operates with clear, certain and accessible rules which find their basis in the fundamental boundaries laid down in constitutional law, Austrian law, as demonstrated earlier, relies on expressing its prohibitions on the vague and uncertain concept of "viable cells", and its prohibitions already suffer from rather weak support from the applicable constitutional requirements. Permissive regulatory frameworks, in contrast, face considerably more difficulties in giving effect to their objectives by way of enacting effective and efficient rules. They, when introducing their conditional permissions, need to address a larger number of regulatory issues, such as the development of new bio-legal concepts, the delineation of rights or value-based boundaries, the protection of rights and interests of the persons concerned, the establishment of an operable institutional-procedural framework, and the need to implement in detailed provisions the general bioethical principles applicable to the activities permitted. They need to provide for balancing exercises, for instance that between the interests of research and therapy and the rights and interests of the persons concerned, and ensure that those balancing exercises are carried out in compliance with the prior established, often ethics-based, bio-legal benchmarks.[98] Learning how other regulatory frameworks address generic and technology-specific frames of regulation can enhance the ability of permissive regimes to provide adequate responses to these problems.

Ultimately, as it follows from general dilemmas of technology regulation, the possibility offered by national regulatory variety for improving regulatory

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[97] See the discussion by Hoppe on the regulatory strategy of erecting prohibitive "firewalls" first and introducing subsequently individual exceptions from the thereby introduced prohibitions, Hoppe, "Innovative Tissue Engineering", *supra* n. 14, p. 121.

[98] See, for example, the provisions regulating the donation of supernumerary embryos for research purposes, or the regulation of the creation of research embryos, when that is permitted.

frameworks and their connection with technology through inter-systemic regulatory learning and borrowing, must be exploited with responsibility. Considering that the penultimate objective of regulatory intervention, as stated by the legal measures themselves, is the ensuring of public health protection through the development of novel biomedical therapies in regenerative medicine, the regulatory choices made have an impact on the access of patients to therapies to treat – often previously incurable – diseases. Regulation and its design are thought to influence the speed of therapeutic technologies moving from bench to bedside, thereby determining whether the best technologically possible therapies are available to patients in a way that justice and equity are ensured in the healthcare domain.[99] Furthermore, regulatory learning and borrowing must have regard to the values inherent in law and the rule of law itself.[100] Regulation, even when it is implemented in a volatile technological environment, is expected to provide certainty and clarity, especially as regards the rights and obligations of individuals and of the other stakeholders affected. These qualities must be maintained on the longer run, especially when technological outputs are likely to be realised in long-term research and development processes.

It is unlikely that hard and fast choices will be available to regulators. While generic measures are more likely to be sustainable on the longer term than technology-specific regulation, the overly extensive scope of such measures, their opaqueness and their lack of detail, especially when they are of low regulatory

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[99] See Hoppe, "Innovative Tissue Engineering", *supra* n. 14, p. 124. He argued that on this basis better targeted measures offering multiple, specialised avenues of technological development should be put in place. He, nevertheless, conceded enforcing the earlier mentioned dilemmas of regulatory connection that the success of regulatory intervention assumes that regulation is able to interact with technology in a way that the concepts used in regulation actually correspond with the technology, regulation actually understands the technology itself, and that regulation is actually prepared to address typical and untypical developments in the technological domain.

[100] *Supra* n. 10, 13.

quality, may unjustifiably impede research and the development of new therapies. The main problem with technology-specific measures, which on the positive side enable a comprehensive and informed regulation of technology, is that they may not provide the flexibility necessary for accommodating scientific and technological change. They may also give rise to fragmentation in the regulatory space jeopardising regulatory accessibility and clarity, and creating boundaries between different aspects of the same technology. On this basis, the responsibility which comes with regulation in the biomedical domain, instead of diminishing, increases the need for learning from other regulatory regimes, wherever they may be located on the prohibitive-permissive scale. The experiences as well as the strengths and weaknesses of other regimes enable reflecting upon the operation and the broader impact of national rules, which is all the more necessary considering that conflict and resistance characterise the engagement of the law with the technology and that the choices in this regard must address the difficulties and the inherent contradictions of connecting rules with the technology regulated.