FUNDAMENTAL DISJUNCTIONS IN THE EU LEGAL ORDER ON HUMAN TISSUE, CELLS & ADVANCED REGENERATIVE THERAPIES

Marcella Favale and Aurora Plomer*

ABSTRACT

The unprecedented expansion of EU controls on biological materials under the aegis of the EU's expanding remit on public health has caused a major reshaping of the regulatory landscape of the life-sciences in Member States. This article analyzes the challenges to national and supranational legal orders posed by the integration of ethical norms within the EU Human Tissue and Cells Directive 2004/23/EC and the Advanced Therapies Regulation (EC) 1394/2007. We show how the infiltration of substantive moral norms in morally contested fields of biotechnology is facilitated by the incorporation into the EU legislative texts of fundamental norms such as respect for human dignity contained in the EU Charter of Fundamental Rights and the Council of Europe's Convention on Human Rights and Biomedicine. The first part of the article sets out the constitutional and normative challenges posed by the EU legislative intervention on ethical matters in the field of health and new biotechnologies. The second part examines the substantive content of the integrated fundamental norms highlighting their open-ended and indeterminate character and the areas of overlap and disjunction. The third part introduces an analytical matrix which is deployed to analyze the reach of fundamental norms in shaping the more specific ethical controls in the legislative texts and reveals how the mix of technical and evaluative norms resolves the ethical and constitutional tensions in the EU texts.

Keywords: EU health policy; Human Tissue and Cells Directive; advanced therapies; biotechnology; ethics and health

* Marcella Favale, Research Fellow, Sheffield Institute of Biotechnology, Law and Ethics, University of Sheffield; Aurora Plomer, Chair in Law and Bioethics, University of Sheffield (a.plomer@sheffield.ac.uk). The research for this paper was undertaken as part of a project funded by the Wellcome Trust '*Is there a Future for Patent Ethics Committees*?', http://www.shef.ac.uk/law/sible/projects/wellcome. The authors would like to thank the Wellcome Trust for its generous support in facilitating this work.

§1. INTRODUCTION

The unprecedented expansion of EU controls on biological materials[1] under the aegis of the expanding remit of the EU on public health[2] has caused a major reshaping of the regulatory landscape of the life-sciences in Member States. A considerable body of EU scholarship has described and analyzed the multi-level governance character of EU intervention on health, highlighting the dynamics of hard and soft law regulatory processes in the health field.[3] This article focuses instead on the challenges to the supranational and national legislations posed by the integration of ethical norms within the EU legal framework.

The adoption of two recent pieces of EU legislation, the Human Tissue and Cells Directive 2004/23/EC (hereinafter, EUCTD) and Regulation 1394/2007 of the European Parliament and of The Council on advanced therapy medicinal products (hereinafter the ATR) was the result of prolonged political conflict between the EU law-making institutions over the EU competence to legislate on ethical matters and sustained pressure from within the EU Parliament for the exclusion of specific applications of the new technologies on ethical grounds.[4] Whilst these attempts were ultimately unsuccessful, the final texts are by no-means a gloss-over on ethical norms. We show how the infiltration of substantive moral norms in morally contested fields of biotechnology is facilitated by dualities and disjunctions in the EU legislative texts including the incorporation of the fundamental norms contained in the EU Charter of Fundamental Rights[5] and the Council of Europe's Convention on Human Rights and Biomedicine (Oviedo Convention).[6]

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1 See principally Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004, OJ L 2004 102/48 (on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells), in subsequent footnotes *EUCTD*; Commission Directive 2006/17/EC, OJ L 2006 38/40 (on donation, procurement and testing of human tissue and cells); Commission Directive 2006/86/EC, OJ L 2006 294/32 (on traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells); Regulation (EC) 1394/2007 of the European Parliament and of the Council, OJ L 2007 324/121 (on advanced therapies), amending Directive 2001/83/EC and Regulation (EC) 726/2004, in subsequent footnotes ATR.

2 The areas identified under the Community Public Health Programme 2003–2008 included health information, rapid reaction to health threats and health promotion. After 2008, the strategic areas were enlarged to include population ageing, health treats and new technologies. See the White Paper, *Together for Health: A Strategic Approach for the EU 2008–2013*, COM(2007) 630 final.

3 See for example Hervey, 'The European Union and the Governance of Health Care', in G. de Búrca and J. Scott (eds.), *New Governance and Constitutionalism in the EU and the US,* (Hart, 2006), 179–210.

4 There were over 120 amendments introduced during the passage of the Directive, many directed to the exclusion of research on human embryonic tissue and cells. See Farrell, 'The Body Politic: Ethical Concerns Regulatory Dilemmas and Human Embryonic Stem Cell Research in the European Union', 28(2) *Zeitschrift für Rechtssoziologie* 2 (2007), 215–227.

5 Charter of Fundamental Rights of the European Union, OJ C 2000 364/01.

6 Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo,

The first part of the article sets out the constitutional and normative challenges posed by the EU legislative intervention on ethical matters in the field of health and new biotechnologies. This is instrumental to show the tension between the EU mandate, which severely limits the competence of the EU to import ethical restrictions on social and economically motivated legislation and the growing infiltration of ethical norms in morally contested fields underpinned by 'pan-European' human rights[7] instruments. The second part of the article examines the dualities, disjunctions and indeterminacy inherent in the human rights norms, whilst the third part introduces an analytical matrix which is deployed to expose how the normative tensions are resolved in the EU texts through a mix of technical and normative elements.

§2. THE POLICY CONTEXT FOR EU ACTION ON BIOTECHNOLOGY

The adoption of the EU legislation on human tissue and advanced therapies is part of a wider EU strategic initiative to enlarge the Community's field of intervention on social and economic matters to include health. An analysis of the preceding legislative interventions in the field of health reveals the latent tensions between the legislative imperative to confine the import of ethical restrictions into the legislation and the political pressure to capture and reflect ethical standards through the imposition of EU-wide technical standards on health and safety. Yet, as will be seen, a strategic initiative whose legal basis pointed to the limited competence of the EU to venture beyond harmonization of technical standards to protect public health also carried the potential to act as a vehicle for the adoption of a European-wide substantive framework of rules whose reach extended beyond the prevention of harm to EU citizen's health. In some instances, this resulted in ethical controls on scientific research in the field of technologies being morally contested, in a culturally diverse Europe.

The directives on blood and human tissues and the advanced therapies regulations were adopted as part of the community's strategic goal to contain 'health threats', defined as infectious diseases threatening the health of citizens in Europe.[8] Included amongst these, were the transmission of emerging pathogens and the resurgence of others, as well as enhancing the rapid and co-ordinated response capability to these threats.[9] Since 1993, eight Action Programmes on health have been initiated by the Commission. The

4.IV.1997, ETS n. 164.

7 With this we mean human rights that are likely to have an impact in the EU legislation, because recognised, directly or indirectly, by EU institutions.

8 See the White Paper, *Together for Health: A Strategic Approach for the EU 2008–2013*, COM (2007) 630 final, 23.

9 Ibid. See also, in the overview of the EU Health Strategy, the section on health threats at http://ec.europa.eu/health/ph_threats/threats_en.htm.

identified priorities originally were health promotion, cancer, drug dependence, AIDS and other communicable diseases, health monitoring, rare diseases, accidents and injuries, and pollution-related diseases.[10] They were replaced in 2007 by a new integrated programme adopted by the European Parliament and the Council.[11] The new six year programme set priorities within a threefold framework including health information,[12] health threats and health determinants.[13]

The social context for the adoption of the original programme on 'health threats' was the emergence of HIV and AIDS, the re-emergence of tuberculosis and the appearance of variant Creutzfeldt Jacob Disease.[14] The Commission anticipated that a reduction of morbidity and mortality would follow from the 'added value' of cross-border community surveillance and introduction of strict quality and safety criteria for the handling of substances of human origin.[15] The strategic aim of containing 'health threats' through the adoption of Community-wide technical health and safety standards, pointed to the adoption of legislative measures with a primarily technical orientation.[16] Specifically, the programme adverted to the number of patients in the EU receiving treatments based on biological substances donated by others, including blood, tissues, cells, and whole human organs. Whilst the programme acknowledged the potential high therapeutic value of these substances, the potential risks for the transmission of communicable diseases were also underscored. Community-wide action to contain cross-border threats in this field was justified as contributing to a reduction of risks specifically through the adoption of legislation prescribing uniform European standards of quality and safety of biological substances, in accordance with the EU remit to ensure that 'a high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities.'[17] Yet, the 'technically' motivated legal intervention carried the potential to become a vehicle for importing ethical restrictions on the use of new technologies. The final texts and wording of the substantive norms adopted

10 Decision No 1786/2002/EC of the European Parliament and of the Council of 23 September 2002, OJ L 2002 271/1 (adopting a programme of Community action in the field of public health: 2003–2008).

11 Decision No 1350/2007/EC of the European Parliament and of the Council of 23 October 2007, OJ 2007 L 301/3 (establishing a second programme of Community action in the field of health: 2008–13).

12 Health Information aims to develop and establish health monitoring systems through the development of health indicators and data collection, analysis and dissemination of information on health. See the Community Public Health Programme 2003–2008, in the Decision No 1350/2007/EC, footnote 11.

13 This is a responsibility shared by national authorities and the Commission. See the Commission Staff Working Document, accompanying the White Paper, *Together for Health: A Strategic Approach for the EU 2008–2013*, COM(2007) 630 final, stating at the outset that 'one of the major differences between this Health Strategy and previous strategic documents on health is that it proposes key cooperation mechanisms together with the Member States and stakeholders…'.

14 See the overview of health threats in the EU at http://ec.europa.eu/health/ph_threats/threats_en.htm.

15 See the Commission Staff Working Document above, COM(2007) 630 final, 16.

16 Ibid, 21.

17 EC Treaty, as amended by Amsterdam 1997, OJ C 1997 340/145, Article 152(1).

reveal precisely such an infiltration of ethical norms but in a form which reflects the constitutional and political tensions in the realization of the EU mandate.

A. THE CONSTITUTIONAL CHALLENGE[18]

The legal basis of EU legislation in the life-sciences field is attributed to the 'Public Health' remit vested on the Community by the EC Treaties.[19] Under Article 152 of the Treaty of Amsterdam[20] the Community is obliged to ensure that 'a high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities.'[21] The measures taken by the Community 'shall complement national policies', '… shall be directed towards improving public health, preventing human illness and diseases, and obviating sources of danger to human health.'[22] The Council is mandated to achieve the objectives referred to in Article 152 EC through adopting measures setting high standards of quality and safety of organs and substances of human origin, blood and blood derivatives.[23] Equally, the mandate of the EU to harmonize national laws, let alone national moral norms in the field of public health, is limited by the overarching principles of the Treaties.[24] Yet, whilst the EU is competent to legislate and harmonize laws in order to facilitate economic integration through the creation of an internal market to facilitate the freedom of movement of people, goods and services, the EU is also bound to respect the national identities of Member States.[25] Article 6 of the EU Treaty[26] emphasizes that the EU is founded on the principles of liberty and democracy[27] and shall respect the constitutional traditions of Member States[28] as well as their national identities.[29] Furthermore, in areas which do not fall within its exclusive competence the principle of subsidiarity requires that the Union should only act when the proposed objectives cannot be sufficiently achieved by the Member States and can be better achieved by the Community.[30] The principle of

18 The term 'constitutional' here is use broadly to refer to the set of rules that govern the EU system, exercise of the EU institutions authority and relations between the EU and Member States.

19 Ex Article 129 EC (Maastricht 1992, OJ C 1992 19/1).

20 Article 152 EC has a wider scope than Article 129 EC. Among the areas of cooperation between member states, the new article lists not only diseases and major health threats but also, more generally, all causes of danger to human health, as well as the general objective of improving health.

21 EC Treaty amended by Amsterdam 1997 OJ C 1997 340/145, Article 152(1).

22 Ibid.

23 Although these measures shall not prevent any Member State from maintaining or introducing more stringent protective measures; ibid, Article 152 (4a) EC.

24 Notably Article 5 of the EC Treaty (Maastricht 1992, OJ C 1992 191/1).

25 EC Treaty amended by Amsterdam 1997, OJ C 1997 340/145, Article 6(3).

26 EC Treaty amended by Amsterdam 1997, OJ C 1997 340/145.

27 Ibid, Article 6(1).

28 Ibid, Article 6(2).

29 Ibid, Article 6(3).

30 EC Treaty (Maastricht 1992, OJ C 1992 191/1), Article 5.

proportionality also requires that any action by the Community shall not go beyond what is necessary to achieve the objectives of this Treaty.[31] As the Union is founded primarily on the economic goal of facilitating the expansion of a free market through the lifting of territorial and cross-border barriers to trade, there is no legal basis under the Treaties for concerted EU action aiming directly at harmonization and unification of national moral norms.[32] Thus, legislative measures adopted by the EU are subordinate to the goal of economic (and to some degree social integration too)[33] but not moral integration, itself subject to the principles of subsidiarity and proportionality.

Yet, the legal reality as to the possible intrusion of moral norms into EU law is somewhat more complex, since moral norms may nevertheless be indirectly incorporated into EU law whose primary goal is to facilitate economic and social integration through a variety of direct and indirect legal means, in addition to extra-legal means such as the funding of research under the EU Research Framework Program.[34] In particular, indirect legal integration or approximation of moral norms may, for instance, be achieved through the incorporation of human rights instruments in the EU Lisbon Treaty,[35] the Opinions of the European Group on Ethics, and the jurisprudence of the European Court of Justice. Alternatively, or in addition, legislative instruments may contain ethically or morally oriented provisions which are ancillary to the goal of achieving freedom of goods and services, albeit subject to the overarching legal requirement to respect the national identity of Member States. This includes the right of Member States to protect their national identity through the adoption of measures involving restrictions on movement of goods or services in order to protect constitutionally enshrined values (Article 30[36]). Hence, the assimilation of moral norms within the EU constitutional fabric carries the potential to expose and heighten tensions in the balance between the EU's prerogative to impose uniform standards in the Community and the degree of autonomy retained by Member States. The resolution of these tensions in the texts, we argue, is effected through the incorporation of overlapping, indeterminate and diverging pan-European fundamental norms and a combination of more specific technical and normative elements explored through an analytical matrix in section 4.

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31 Ibid.

32 Unlike the Council of Europe, for instance, the European Union's aim is not to 'achieve greater unity between its members for the purpose of safeguarding and realising the ideals and principles which are common to their heritage'. See Article 1, Chapter 1, Statute of the Council of Europe (1949), ETS n. 001. Economic and social progress are also stated as additional objectives, but with no indication of any particular economic orientation.

33 For example D. Dinan, *Ever Closer Union,* (Palgrave MacMillan, 2005), see generally Chapter 14.

34 Hervey, 'The European Union and the Governance of Health Care', 197.

35 EC Treaty, as amended by Lisbon 2007, OJ C 2008 115/13, Article 2.

36 See the consolidated version of the Treaty on the functioning of the European Union, OJ C 2008 115/47, Article 36 (ex Article 30 TEC): 'The provisions of Articles 34 and 35 shall not preclude prohibitions or restrictions on imports, exports or goods in transit justified on grounds of public morality, public policy or public security; the protection of health and life of humans, animals or plants; …'.

B. THE NORMATIVE CHALLENGE

The identification of European-wide moral norms consistent with the plurality and diversity of ethical cultures in Europe poses a formidable challenge for the drafting of specific legislation in morally contested fields such as the regulation of new technologies on human tissue, cells and advanced therapies. There are deep social and cultural divisions in Europe, and indeed within the EU Member States on morally sensitive issues such as the use of certain types of human tissue or cells for therapeutic purposes. The controversies are focused to a large extent, but not exclusively, on the use of human embryonic cells, with considerable opposition within large sectors of European states to such uses.[37] Aside from the controversies relating to the exclusion of certain types of tissues or cells, there is as yet no consensus in Europe either on the requirements of 'informed' consent, whether the consent should be generic or specific and specifically whether donors should be able to veto or dictate the use of donated tissue. The aspiration to offer a distinctive 'European' answer to and resolution of these normative questions thus poses a number of challenges.

In the first instance, the formulation of a distinctively European ethic must avoid the charge of ethnic/sectional/regional bias. One of the difficulties with the idea of a distinctive *European* regional morality,[38] as opposed to a set of legally recognized and enforceable norms amongst EU Member States, is that the European ideal seems *prima-facie* potentially inconsistent with the aspiration to universality of ethical and moral discourse.[39] Ethical norms and principles are characteristically unbounded by ethnic, territorial or temporal limits.[40] This is reflected in the language of ethical codes and legal instruments imposing duties or vesting rights on 'everyone', 'each individual', 'no person', irrespective of geographical location in space or time, both in international instruments such as the Universal Declaration on Human Rights and in European instruments.[41] For instance, Article 2 of the ECHR proclaims that 'Everyone has a right to life' whilst Article 14 of the ECHR underscores the universal reach of the provision with the requirement that the rights in question '… shall be secured without discrimination on any ground such as sex, race, colour, language, religion, political or other opinion, national or social origin, association with a national minority, property, birth or other status.'[42]

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37 See *infra*, §4, sections B and C.

38 To be captured, for instance, by institutions such as the European Group on Ethics.

39 See generally, for instance, R. Macklin, *Against Relativism: Cultural Diversity and the Search for Ethical Universals in Medicine*, (OUP, 1999).

40 Acknowledgement of the universal character of moral norms in no way involves a denial of cultural and social diversity. As noted by Macklin, empirical facts disclosing variations between cultures and societies do not compel the conclusion that what is right or wrong can be determined only by the beliefs and practices within particular cultures: R. Macklin, *Against Relativism*, (OUP, 1999), 178.

41 See generally O. O'Neill, *Loosening the Bounds of Human Rights Global Justice and the Theory of Justice*, *(*CUP, 2000).

42 Article 2 of the UNDHR similarly proclaims that '… no distinction shall be made on the basis of the political, jurisdictional or international status of the country or territory to which a person belongs,

Just as there are serious conceptual difficulties in elucidating the meaning of European citizenship without importing exclusionary and discriminatory sectarian racial and national criteria, there are parallel challenges in the identification and elaboration of a set of moral norms which are distinctively 'European'.[43]

Secondly, the search for overarching ethical values cutting across the diversity of European cultures carries the risk of generating principles at a level of generality which potentially divests or empties them of any substantive content or meaning.[44] Overarching fundamental values such as human dignity embedded in international and regional instruments have famously been dismissed by scholars as empty or 'useless' and open to judicial manipulation.[45] Both the EUCTD and ATR endorse directly or indirectly fundamental principles and norms such as 'human dignity' and autonomy.[46] A crucial question is to what extent the fundamental overarching ethical principles in the EU legislative instruments are accompanied by and reflected in concrete, non-empty provisions imposing meaningful specific legal obligations on EU Member States.

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whether it be independent, trust, non-self-governing or under any other limitation of sovereignty.' For a detailed discussion of the universal character and reach of human rights principles in the field of research trials in developing countries, see generally Fidler, '"Geographical Morality" Revisited: International Relations, International Law, and the Controversy Over Placebo-Controlled HIV Clinical Trials in Developing Countries', 42 *Harvard International Law Journal* 299 (2001).

43 For a sustained critique of the potential undertone of exclusions and discrimination lurking in the concept of European citizenship see generally: E. Balibar, *We the People of Europe? Reflections on Transnational Citizenship*, (Princeton University Press, 2004). The Lisbon Treaty will for the first time allow the EU to accede to the Council of Europe, and therefore provide a legal basis for the jurisprudence of the ECtHR to be binding on the EU. So, the effect of the Lisbon Treaty is arguably to enhance the status of the ECHR. However, the complication arises from the parallel recognition of the Charter, whose jurisdiction falls on the ECJ (which, incidentally, had hitherto freely drawn from the jurisprudence of the ECtHR). Juridically, this creates the potential for disjunction and conflict, as indeed has been noted by this commentator. The EU's legal value is encapsulated in what is conceived as a form of metaconstiutionality, which is to ensure political cohesiveness of the Union, should be emphasized here. In line with Habermas' thinking, the broader purpose of the metaconsitutional structure in not a creation of anything beyond the historical capacity of the human intellect, but a conservation of the 'great democratic achievement of the European nation-state, beyond its own limits'. See Habermas, 'Why Europe Needs a Constitution', 11 *New Left Review* 5 (2001), 6.

44 This is a problem attached to the elaboration of principles or norms at a high level of generality. See generally A. Plomer, *The Law and Ethics of Medical Research: International Bioethics and Human Rights*, (Routledge-Cavendish, 2005) and R. Macklin, *Against Relativism,* (OUP, 1999).

45 See generally for instance, Macklin, 'Dignity is a useless concept', 327 *BMJ* (2003), 1419–1420; and Ashcroft, 'Making Sense of Dignity', 31 *Journal of Medical Ethics* 11 (2005), 679–682. Whilst Christopher McCrudden has argued that the concept of human dignity does not provide a principled basis for judicial understanding in the sense that there is little understanding of what human dignity requires substantively: McCrudden, 'Human Dignity and Judicial Interpretation of Human Rights', 19 *European Journal of International Law* 4 (2008), 655–657. For a defence of the principle, see Pellegrino, 'The Lived Experience of Human Dignity', in *Human Dignity and Bioethics: Essays Commissioned by the President's Council on Bioethics* (The President's Council on Bioethics Washington, D.C. March 2008), available at http://www.bioethics.gov/reports/human_dignity/chapter20.html.

46 See infra § 3.

A further complication arises from the fact that the EU legislative instruments refer to a number of regional instruments whose substantive normative content is not identical. This includes notably the Council of Europe's Convention on Human Rights (1950)[47], the Council of Europe's Convention on Human Rights and Biomedicine (1997)[48] and the EU Charter of Fundamental Rights (2000).[49] Yet, the inclusion in an EU legislative text of instruments adopted separately by the EU and the Council of Europe, obscures the duality of jurisdiction between the European Court of Justice (over the Charter) and the European Court of Human Rights (over the Council of Europe's Treaties) and the potential for legal and normative disjunctions on the authoritative interpretation of the principles and rights protected under each instrument.[50] The jurisdictional duality is of special significance because it carries the potential to exacerbate further the existing normative disjunctions, indeterminacies and ambiguities in the substantive principles formulated in the separate instruments, which are further analyzed in the next section.[51]

§3. FUNDAMENTAL NORMS AND DISJUNCTIONS IN EUROPEAN HUMAN RIGHTS INSTRUMENTS

A close analysis of the fundamental norms contained in the European human rights instruments incorporated in EU legislative texts reveals the inherent ambiguities, overlap and disjunctions in the substantive content of norms such as human dignity, bodily integrity and prohibition on financial gain, guiding the interpretation of the more specific or second order ethical constraints such as consent on uses of human tissue, cells and advanced therapies specified in the Directive and Regulations. In this section, we focus specifically on the human rights instruments expressly acknowledged in the EUCTD and ATR, notably the Oviedo Convention (Section A) and the EU Charter of Fundamental Rights (Section B). We show how the reaching of a moral consensus on first order, overarching fundamental principles such as human dignity is facilitated by the incorporation of indeterminate and open-ended moral norms preserving the right of member states to align the moral parameters of local and national moral cultures on uses of human tissue and cells to the fundamental norms. In Section 3, we show how these

47 Convention for the Protection of Human Rights and Fundamental Freedoms as amended by Protocol No. 11, Rome, 4 November 1950, ETS n. 005.

48 Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo, 4 April 1997, ETS n. 164.

49 Charter of Fundamental Rights of the European Union, OJ C 2000 364/01.

50 See generally Williams, 'The (Im)Possibility of the European Union as a Global Human Rights Regime', in R. Brownsword (ed.), *Global Governance and the Quest for Justice,* (OUP, 2004). Also, S. C. Greer, *The European Convention on Human Rights: Achievements, Problems and Prospects*, (CUP, 2006).

51 Ratification of the Lisbon Treaty is not a foregone conclusion. At the time of writing, for example, a referendum in Ireland had rejected the ratification of the Treaty. Negotiations to 'rectify' the outcome of the referendum are still under way.

first order fundamental principles guide the flexible interpretation of the more specific second order ethical norms contained in the legislative texts and combine with technical controls analyzed through the lens of an analytical matrix deployed in section 4.

According to the European Commission, the Human Tissue and Cells Directive 2004/23/EC (hereafter, the EUCTD)[52] was adopted after extensive consultation with institutions like the Council of Europe and the World Health Organization and was intended to be consistent with a range of human rights instruments in the field.[53] The preamble to the EUCTD specifically recalls the European Convention of Human Rights (1950), and states that the Oviedo Convention[54] and additional protocols are 'taken into account', whilst the substantive provisions are intended to be 'consistent with' the Charter of Fundamental Rights of the European Union.[55] Similarly, the Advanced Therapies Regulation 2007 (hereafter, the ATR)[56] proclaims respect for the fundamental rights and observance of the principles reflected in the Charter of Fundamental Rights of the European Union and 'takes into account' the Oviedo Convention.[57] These different wordings could indicate that the Charter's 'guiding influence' takes priority over the Oviedo Convention and its protocols; the provisions in the Directive and Regulations are expressly intended to be 'consistent with' or 'observe' and 'respect' the rights enshrined in the Charter but not necessarily those enshrined in the Convention which they have merely 'taken into account'. The enhanced status of the Charter vis-à-vis the Convention is further reinforced in the subsequent Commission Directive on quality and safety procedures which, as well, recalls only the Charter.[58]

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52 EUCTD.

53 See Commission Directive 2006/17/EC, OJ L 2006 38/40, Recital 6: 'This Directive is based on international experience drawn upon through an extensive consultation, the Council of Europe's Guide to safety and quality assurance for organs, tissues and cells, the European Convention on Human Rights, the Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo, 4.IV.1997), with its additional protocols, and recommendations from the World Health Organization. In particular, with regard to further additional biological testing for donors originating from high-incidence areas of specific diseases or whose sexual partners or parents originate from high-incidence areas, Member States will refer to existing international scientific evidence. The Directive is consistent with the fundamental principles set out in the European Charter of Fundamental Rights.'

54 Convention for the Protection of Human Rights and Dignity of the Human Being with regard to Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo, 4.IV.1997), ETS n. 164.

55 EUCTD, Recital 22. The Directive also recognizes the role of the opinions of European Group on Ethics in Science and New Technologies (EGE) in evaluating all ethical aspects of biotechnology. The Directive states that EGE's opinions have been taken into account while drafting the Directive (Recital 33).

56 Regulation (EC) 1394/2007 of the European Parliament and of The Council, OJ L 2007 324/121 (on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) 726/2004).

57 ATR, Preamble, Article 8.

58 See Commission Directive 2006/86/EC, OJ L 2006 294/32, Recital 12: 'This Directive respects the fundamental rights and observes the principles recognised in particular by the Charter of Fundamental

Whether or not there is an intended hierarchy, the fundamental norms enshrined in both the Council of Europe's human rights instruments and the EU Charter, as will be seen, are central to the interpretation of the more specific, second order ethical values contained in the EU legislation further analysed in Section 4. The analysis of the fundamental norms underpinning these instruments discloses the ambiguities and disjunctions in the key fundamental norms.

A. THE COUNCIL OF EUROPE CONVENTION ON HUMAN RIGHTS & BIOMEDICINE

The overarching fundamental or higher order values asserted in Chapter I of the Council of Europe Convention on Human Rights and Biomedicine (Oviedo Convention) include ' the dignity and identity of all human beings', the non-discrimination and respect for integrity, and other rights and fundamental freedoms with regard to the application of biology and medicine' (Article 1). The primacy of the human being over the sole interests of science (Article 2), the equitable access to health care (Article 3) and the requirement that any intervention in the health field should be carried out in accordance with relevant professional obligations and standards (Article 4). More specific, 'second-order' values are detailed in the ensuing chapters: specifically, 'Consent' (Chapter II), 'Privacy and right to information' (Chapter III), 'Organ and Tissue Removal' (Chapter IV) and prohibition of financial gain (Chapter X). The specific rules in each chapter have to be read consistently with the statement of general values and purpose of the Convention stated in the first Chapter of the Convention.[59]

According to the explanatory report: 'The concept of human dignity … constitutes the essential value to be upheld. It is the basis of most of the values in the Convention.'[60]

Yet the concept of human dignity, although central to the ECHR and international human rights instrument generally, is to a large extent under-determined and open to conflicting interpretations depending on whether it is grounded in the individual's capacity to make autonomous choices, thus entailing that respect for human dignity requires respect for the individual's exercise of autonomous choices (human dignity as liberty/empowerment)[61] or alternatively whether human dignity is grounded in natural

Rights of the European Union.'.

59 Note that the drafting committee agreed that the term 'human being' should be understood in its widest sense and avoided the inclusion in the framework Convention of a definition of the human being; they also did not specify whether the framework Convention applies to the human being only after birth or also before, and whether the framework Convention also applies to gametes and genetic engineering; they did not to include a definition of bioethics, the difference between the latter and medical deontology being sufficiently well established. Nevertheless, the explanatory report gives some details on the concept of bioethics. See Explanatory Report to Oviedo Convention, DIR/JUR (97)5, 5.

60 Ibid, para.10.

61 The core idea was originally advanced by I. Kant, *Groundwork of the Metaphysics of Morals*, (Wilder, 2008) and developed in the twentieth century in A. Gewirth, *Reason and Morality*, (University

attributes of the individual or human species imposing an obligation not to alter or modify human life (human dignity as constraint).[62] This second reading of human dignity as constraint is evident in the explanation of the drafters of the Oviedo Convention that many of the current advances of science, particularly genetics, pose a risk not only to the individual himself or society, but to the human species. Hence, the explanatory report states 'the Convention sets up safeguards, starting with the preamble where reference is made to the benefits of future generations and to all humanity, while provision is made throughout the text for the necessary legal guarantees to protect the identity the human being.[63] The dual and contrasting liberal and paternalistic meanings of 'human dignity' present in the Oviedo Convention reflect a similar duality in third generation human rights instruments such as UNESCO Declaration on the Human Genome[64] and the latest UNESCO Declaration on Bioethics.[65]

The two contrasting conceptions of human dignity have radically opposed implications for the framing of EU ethical norms on biotechnology, depending on whether the libertarian or paternalistic perspective is followed. For instance, the requirement for the informed consent in Article 5 or privacy and right to information in Article 10 of the Oviedo Convention may be rooted in the higher-order value and overarching requirement to respect human dignity, where human dignity is understood in liberal terms as a fundamental principle requiring respect for the capacity of individuals to make autonomous choices.[66] On the other hand, the prohibition on financial gain in Article 21 sets constraints on organ and tissue removal in Article 19 and the exclusions and limits on uses of human embryos for research purposes in Article 18, are arguably

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of Chicago, 1978). Neo-Kantian applications to new biotechnologies include D. Beyleveld and R. Brownsword, *Human Dignity in Bioethics and Biolaw,* (OUP, 2001).

62 For an incisive analysis of the contrast between human dignity as empowerment and human dignity as constraint, see generally Feldman, 'Human Dignity as a Legal Value', *Public Law* (1999), 682–702. See also Wheatley, 'Human Rights and Human Dignity in the Resolution of Certain Ethical Questions in Biomedicine', 3 *European Human Rights Law Review* (2001), 312–325.

63 Explanatory Report to the ECHRB, DIR/JUR (97) 5, para. 14; see records of the general conference of Paris, 21 October to 12 November 1997 (UNESCO 1998), available at: http://portal.unesco.org/en/ev.php-URL_ID=13177&URL_DO=DO_TOPIC&URL_SECTION=201.html. In ascribing rights and dignity to the human species as a whole, the Council of Europe's Convention on Human Rights and Biomedicine stands apart from both first and second generation human rights instruments, which have traditionally sought to protect the negative and positive socio-economic rights of individuals and society, respectively.

64 Where there are no less than 16 references to human dignity. See Feldman, 'Human Dignity as a Legal Value', 682–702.

65 See Records of the general conference of 19th October 2005 (UNESCO 2006), available at http://unesdoc.unesco.org/images/0014/001461/146180E.pdf.

66 As the Explanatory Report states, this Article deals with consent and affirms at the international level an already well-established rule, that no one may in principle be forced to undergo an intervention without his or her consent. Human beings must therefore be able freely to give or refuse their consent to any intervention involving their person. This rule makes clear patients' autonomy in their relationship with health care professionals and restrains the paternalist approaches that ignore the wish of the patient. See the Explanatory Report to the ECHRB, DIR/JUR (97) 5, para. 34.

grounded on a paternalistic understanding of human dignity justifying State interference with an individual's autonomous choice either to protect the individual from himself or to uphold values said to be inherent in a human being or the human species as a whole.

B. THE EU CHARTER ON FUNDAMENTAL RIGHTS

The EU Charter of Fundamental Rights[67] is both structurally and in terms of content different from the Oviedo Convention as regards the fundamental values identified and their ordering. The preamble to the EU Charter states that the Union is founded on the indivisible, universal values of human dignity, freedom, equality and solidarity and emphasizes that the goal of developing these common values is to be pursued alongside respect for diversity of cultures and constitutional traditions of Member States.

The Charter is divided into six chapters 'Dignity', 'Freedom', 'Equality', 'Solidarity', 'Justice', 'Citizens Rights'. The counterpart norms to those in the Oviedo Convention come mostly under the umbrella of the chapter entitled 'Dignity' which, in other leading human rights instruments is traditionally part of the Preamble.[68] By contrast, human dignity in the Charter is enshrined in Article 1 of the text, stating that human dignity is inviolable and must be respected. Whilst this could be read as signifying that human dignity is to be treated a right in itself,[69] in the absence of further specific obligations flowing from the right[70] and the Preamble's alignment of human dignity with other universal values of freedom, equality and subsidiarity, the more natural reading instead is that human dignity is to be understood as the overarching value underlying the more specific rights or second order values detailed under the chapter of the same name. These include the 'Right to Life' (Article 2), the 'Right to the Integrity of the Person' (Article 3) and the prohibition of torture (Article 4) and slavery (Article 5). Article 2 of the Charter is based on the same provision as Article 2 of the ECHR.[71]

By contrast, Article 3 introduces a distinct right to integrity of the person without direct counterpart in the Oviedo Convention or the ECHR.[72] At the same time, the right

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67 Charter of Fundamental Rights of the European Union, OJ C 2000 364/01.

68 For instance, the 1948 Universal Declaration of Human Rights enshrined this principle in its preamble, first paragraph: 'Whereas recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family is the foundation of freedom, justice and peace in the world'.

69 As suggested, in the explanatory notes: 'The dignity of the human person is not only a fundamental right in itself but constitutes the real basis of fundamental rights'. See the Explanations Relating to the Charter of Fundamental Rights, OJ C 2007 303/17.

70 Feldman, 'Human Dignity as a Legal Value', 682–702.

71 Explanatory Report to the ECHRB, DIR/JUR (97) 5, 7.

72 ECHR, Article 3 – Right to the integrity of the person. 1. Everyone has the right to respect for his or her physical and mental integrity. 2. In the fields of medicine and biology, the following must be respected in particular: the free and informed consent of the person concerned, according to the procedures laid down by law, the prohibition of eugenic practices, in particular those aiming at the selection of persons, the prohibition on making the human body and its parts as such a source of financial gain, the prohibition of the reproductive cloning of human beings.

to integrity enshrined in Article 3 captures some of the rights specified in the Convention under separate discrete clauses. The consent requirement in Article 3(2) of the Charter maps unto Article 5 of the Oviedo Convention prescribing the need to obtain a person's free and informed consent before any intervention in the health field. The prohibition on making the human body and its parts a source of financial gain mirrors exactly Article 21 of the Convention, whilst the prohibition of reproductive cloning of human beings has no direct counterpoint in it. Instead the counterpart is to be found in the protocol of the Oviedo Convention.[73] Thus, the rights subsumed in the Chapter 1 of the EU Charter, on human dignity, reflect the ambivalent dual nature of the principle in the Oviedo Convention both facilitating individual choice through the right to informed consent but constraining individual autonomy through restraints on commercialization of the human body and excluded uses of reproductive technologies. Significantly, the right to privacy and protection of personal data in the Charter is subsumed under the Chapter on Freedoms.

§4. ANALYTICAL MATRIX

From a constitutional perspective, the more specific and determinate the formulation of fundamental principles and rights enumerated in the Charter, ECHR and Oviedo Convention, the greater the degree of moral convergence or integration required amongst the varying moral and legal cultures of Member States of the European Union. Conversely, the more open-ended the formulation, the greater the margin of discretion left to Member States to align their distinctive moral and legal cultures to the enumerated general principles.[74] For instance, the prohibition on cloning in Article 3(1)2 of the EU Charter extends only to *reproductive* cloning, reflecting the unanimous view of Member States, but not to *therapeutic* cloning on which Member States are divided. Thus, the bar for exclusion of contested technologies on ethical grounds is very high, as it requires a high degree of normative convergence between the moral cultures of Member States. Conversely, general and open-ended principles and norms facilitate the co-existence of a diversity of more specific norms and rules reflecting the different national moral and legal traditions of member states.

In this light, it is not surprising that the 'higher-order' fundamental ethical values of freedom/autonomy and dignity in the Charter and Oviedo Convention are mirrored, but only in part, in the texts of these EU Directive and Regulations. The modulating factor is

73 Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings (1998), ETS n. 168.

74 See for instance the (controversial) Declaration on Human Cloning, adopted in UN General Assembly, resolution 56/93 of 12 December 2001 (United Nations Declaration on Human Cloning A/RES/59/280).

the tension between the limits to the EU mandate, which is not supposed to harmonize ethical standards and the growing pressure of fundamental principles, as reflected by the express acknowledgement of human rights codifications in the preambles of the EUCTD and the ATR. As a result, the ethical norms contained in the EUCTD and ATR can be analyzed according to a tri-partite matrix along two axes reflecting the level of prescription of EU norms (viz. from strictly mandatory to optional) and the degree of normative variability permitted (viz. from uniform to flexible).

A. THE REGULATORY MATRIX

The form and content of ethical norms contained in the EUCTD and ATR can be analyzed according to a tri-partite matrix identifying the mix of ethical or evaluative/non-evaluative elements in the texts. At one end of the spectrum, the EUCTD and the ATR introduce EU-wide ethically motivated[75] but essentially scientific technical, uniform standards which are fixed and are strictly obligatory.[76] At the other end of the spectrum norm or value based, 'ethics' driven regulation in transnational contexts sets standards and norms in an open-ended, aspirational, flexible form allowing for a high degree of variability in the interpretation and determination of specific rules or norms in order to accommodate a plurality and diversity of ethical perspectives. In between strict, measurable uniform standards and aspirational open-ended norms/values, a middle third way involves a mix of mandatory but loosely constrained, open-ended, flexible ethical norms. The character of the controls introduced the EU texts may be analyzed against the matrix to reveal the mix of ethical and non-ethical controls. The tri-partite matrix may thus be mapped against the following regulatory modes:

1. Techno-Regulation

The underlying regulatory model in this case aims to be 'value-neutral' and freed from the variability and uncertainty attending ethical, political or social values. The goal is to rationalize, manage and control harm to health through the adoption of uniform, scientific and value-free 'risk-based' standards. The ultimate ambition is to facilitate the development of measurable indicators and uniform detailed technical rules or procedures transcending national boundaries and ensuring compliance within a sector.[77] Standards

75 Viz. protection of public health.

76 See infra: Techno-Regulation.

77 Yet, the comparative histories of risk-based regulation in the developed economies of the US, UK and Germany, suggests that the view of risk-based regulation as a complete value-free enterprise is somewhat removed from the complex reality. In the case of GM crops, in particular, the boundary between scientific 'facts' and political/social values has proved to be less hard and more permeable than the ideal model suggests.

are strictly enforceable and mandatory and typically enforceable through regulatory agencies.

2. Higher-Order Normative Regulation

By contrast, 'normative regulation' is based on ethical, political or social values attended with different degrees of variability. At one end of the spectrum, normative principles may be open-ended, moral, aspirational ideals, of potentially fuzzy and indeterminate semantic application. Higher-order fundamental values such as equality, solidarity or dignity specified in the Preamble or non-binding part of international or regional human rights instruments are the clearest examples.[78] Often, such general and open-ended ethical norms are legally 'soft' and even when contained in binding part of the legal instrument may allow for considerable flexibility in the interpretation and determination of specific obligations.[79]

3. Second-Order Normative Regulation (Mixed)

'Second-order' values specify more determinate ethical norms which are derivative from higher-order norms or principles. Their form or content is therefore less open-ended and may constrain but in a flexible form. For instance, ethical norms such as consent requirements or data protection are typically derivative from the higher-order overarching principles of freedom/autonomy or human dignity, but the precise determination, content or form of implementation may be left open. The matrix table thus looks like this:

Matrix Table

Higher-Order Normative Regulation	Optional/Open-Ended	Flexible
Second-Order Normative Regulation	▲ Mixed ▼	▲ Mixed ▼
Techno-Regulation	Compulsory/Binding	Rigid

An analysis of the ethical controls in EUCTD and of the ATR according to the above matrix reveals the regulatory and legislative mix relied upon by the EU to navigate

78 For example, the Preamble to Charter states that 'the Union is founded on the indivisible, universal values of human dignity, freedom, equality and solidarity'.

79 See *infra*, section B.

through and resolve the potential tensions in the integration of a morally and culturally diverse Europe.

B. HUMAN TISSUE DIRECTIVE (2004/23/EC)

Concerns over the lack of a regulatory framework at EU level on medical uses of human tissue began to emerge in 1998 in the context of the adoption of the EU Directive on *in vitro* diagnostic medical devices[80] which excluded human viable tissue from its scope. There were three reasons justifying the exclusion: a) the lack of control at procurement level; b) lack of authorization and inspection of the establishment involved in tissue and cell's procurement; c) and non-binding standards on quality and safety of the biological material. On that occasion the Commission stressed the need for specific legislation in the field. Moreover, the European Group on Ethics in the same year also declared the need to regulate the way tissue and cells circulate in the internal market, although on ethical basis. The first draft of the Directive was issued in 2002 and the final text adopted in 2004. The Directive applies 'to tissues and cells including haematopoietic peripheral blood, umbilical-cord (blood) and bone-marrow stem cells, reproductive cells (eggs, sperm), foetal tissues and cells and adult and embryonic stem cells'.[81] It does not apply to a) 'autologous draft within the same surgical procedure', b) blood and blood cells, c) organs. It expressly excludes from its remit *in vitro* research.[82]

The Directive had a turbulent passage through the EU Parliament, when a coalition of MPs primarily from the Christian Democrat and Green groups attempted to insert into the legislation amendments banning embryonic stem cell applied research and tissue transplants involving material derived from embryonic stem cells. The amendments highlighted to divisions and contested nature of the European moral norms on embryo research. The attempts to exclude and restrain uses of this technology in the Directive, on the basis of respect for human dignity, were ultimately narrowly defeated.[83]

By contrast, differences amongst Member States on restraints regarding payment for tissues or cells were neutralized in the Directive through the adoption of a general open-ended norm enjoining Member States to 'take the necessary measures to encourage voluntary and unpaid donations of human tissues and cells with a view to ensuring that, insofar as is possible, they are obtained from such donations'. As Farrell notes, the significant shift lies in the alteration from the original mandatory language stipulating

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80 Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998, OJ L 1998 331/1 (on in vitro diagnostic medical devices).

81 EUCTD, Recital 7.

82 EUCTD, Recital 11: 'does not cover research using human tissues and cells […outside the human body…] e.g. in vitro research or in animal models'.

83 See the Report on the EUCTD proposal, 25 March 2003, final A5–0103/2003. Most of 'ethical' amendment herein proposed by the Parliament were rejected. In particular, see Amendment 14, which suggests 'Member States should try to create a code of conduct…[that provides for]… a ban on producing human embryos with the same genetic data as another human being'.

that Member States 'shall take' the necessary measures to encourage voluntary donations, to the aspiration that States 'shall endeavour' to take the necessary measures. This is the clearest example of the aspirational type of regulation, as described by the previous section.

On the other hand, the Directive introduces mandatory, uniform and fixed norms in relation to safety standards for the procurement of human tissue and cells, destined to human application. It stipulates the obligations of the authorities within Member States, like supervision of the procurement process, accreditation, designation, authorization or licensing of tissue establishments, inspections and controls, traceability, import/export of human tissues and cells, registration of establishments, notification of serious adverse events and reactions.[84] It further sets provisions for the quality and safety of tissue and cells, and it set requirements for the responsible person, the personnel, tissue and cell reception, and processing and storage. Moreover, it adds labelling requirements and rules on the relationship between the establishment and third parties.[85] Finally, the Directive tackles exchange of information between member states and the EU Commission, reports and penalties regarding the implementation of the Directive[86] and deals with the committees, which, at the same way as in the Blood Directive, are mandated to issue detailed regulations on the above discipline.[87]

In between the aspirational ideals and the prescriptive technical, health related criteria, the Directive incorporates a number of ethically motivated controls and prescriptive but flexible ethical norms relating to donor selection and data protection.[88] For instance, an annex to the Directive specifies the information to be given to living donors and representatives of deceased donors. There is a noticeable difference between the part A of the Annex, reserved to living donors, and the part B, reserved to deceased donors. Part A details the information that has to be provided to the donor,[89] and stipulates that '[t]he information must be given by a trained person able to transmit it in an appropriate and clear manner, using terms that are easily understood by the donor'.[90] It further states that '[t]he donor must be informed that he/she has the right to receive the confirmed results of the analytical tests, clearly explained'.[91] Conversely, Annex B on deceased donors merely

84 EUCTD, Chapter 2.
85 Ibid., Chapter 4.
86 Ibid., Chapter 5.
87 Ibid., Chapter 6.
88 Ibid., Chapter 3.
89 Ibid., Annex.4. The donor must be informed that he/she has the right to receive the confirmed results of the analytical tests, clearly explained.5. Information must be given on the necessity for requiring the applicable mandatory consent, certification and authorisation in order that the tissue and/or cell procurement can be carried out.
90 Ibid., Annex A.2.
91 EUCTD, Annex A.4.

states that all information and the confirmed results of the analysis of the tissue have to be communicated in accordance with the legislation of Member States.[92]

Moreover, as regards consent, the Human Tissue Directive is supplemented by the EU Commission Directive 2006/17/EC[93] on donation, procurement and testing of human tissue and cells, which sets out detailed requirements to ensure health and safety of both donors and prospective beneficiaries of the relevant therapies. The Commission Directive intended to detail the provision of a Directive of the Parliament and of the Council, mostly stipulates mandatory and uniform norms. However, it also specifies that before the procurement an authorized person must confirm and record that consent has been obtained in accordance with Article 13 of the EUCTD.[94] Article 13 defers to the legislation of Member States on consent. Moreover, the Commission Directive also mandates the legislation of Member States to respect the dispositions of the Annex which, in the case of living donors are detailed as regards form, but in the case of deceased donors are again redirected to the legislation of Member States. In either case, the Directive leaves open the substantive content of the consent requirement as regards the ethically contested question of whether consent as to future uses of the tissue or cells should be generic or specific After a long series of forwarding commands, therefore, the Commission directive leaves part of its regulations open and flexible, for Member States to draft their own legislation.

As for data protection, the Directive asks Member States to take 'all necessary measures' to protect personal data collected in the application of the Directive, and to protect the identity of the donors against recipients and *vice versa*, in observance 'without prejudice to legislation in force in Member States on the conditions for disclosure, notably in the case of gametes donation'.[95] It does not give further details on the nature of those measures, if not with the general indication that data security measures should be in place[96] and procedures are set against the discrepancies of data.[97] As regards consent and protection of personal data, therefore, the EUCTD imposes mandatory norms, but leaves to Member States the detailed determination of the specific obligations. The above shows that the EUCTD tackles the most delicate ethical matters in the parts of the Directive that are the middle ground between open-ended aspirational declarations and prescriptive norms.

92 Ibid., Annex B 1–2.
93 Commission Directive 2006/17/EC, OJ L 2006 38/4.
94 Ibid., Annex 4 1.1.1(a).
95 EUCTD, Article 14.3.
96 Ibid., Article 14.2(a).
97 Ibid., Article 14.2(b).

C. REGULATION ON ADVANCED THERAPIES 1394/2007 AMENDING MEDICINE DIRECTIVE (2001/83/EC)

The new Regulation on Advanced Therapies 2007 (ATR)[98] was adopted to fill another regulatory gap in the complex structuring of EU controls on medicinal products and extends legislation covering pharmaceuticals, medical devices, gene therapy and somatic cell therapy to advanced therapies based on tissue engineering and tissue engineered products. The ATR covers tissue engineered products (TEPs) which fall within the definition of medicinal products, grouping together gene therapy and somatic cell therapy medicinal products as 'advanced therapy medicinal products' (ATMPs).

The new regulation on 'advanced therapy medicinal products' was introduced to fill the gap between the Directive on Medicines (Directive 2001/83/EC)[99] and the EUCTD in order to regulate the use of engineered tissues for therapeutic purposes.[100] In addition to the setting of uniform manufacturing, quality and pharmacovigilance standards to protect EU citizens' health, the Regulations extend to ATMPs the centralized EU procedure for marketing authorization previously applicable to pharmaceuticals[101] through the European Medicines Agency (EMEA).

The new Advanced Therapies Regulation was adopted by the European Parliament in April 2007, approved by the Council on the 30th of May 2007. It is has been in force since 30th December 2008. The passage of the legislation through the European legislative institutions was all but peaceful, with an attempt, once again, to use the Regulations as a vehicle to exclude morally contested biotechnologies. The Committee for Legal Affair (JURE) proposed several amendments, among which two particularly controversial. Amendment 17, reciting:

> This Regulation shall not apply to advanced therapy medicinal products that contain or are derived from human embryonic or foetal cells, primordial germ cells or cells derived from those cells.[102]

And Amendment 3, stating:

> This Regulation should prohibit any authorisation of products derived from human-animal hybrids or chimeras or containing tissues or cells originating or derived from human-animal

98 ATR.

99 Directive 2001/83/EC of The European Parliament and of the Council of 6 November 2001, OJ L 2004 311/67 (on the Community Code relating to Medicinal Products for Human Use).

100 Proposal for a Regulation of the European Parliament and of the Council on Advanced Therapy Medicinal Products and amending Directive 2001/83/EC and Regulation (EC) 726/2004, COM(2005) 567 final.

101 Commission Directive 2003/94/EC, OJ L 2005 91/13 (setting manufacturing requirements to be applied to investigational medicinal products) and Regulation (EC) 726/2004 of the European Parliament and of the Council, OJ L 2004 136/1.

102 Report on the ATR proposal, A6–0031/2007 final.

> hybrids or chimeras. This provision should not exclude the transplantation of somatic animal cells or tissues to the human body for therapeutic purposes, in so far as it does not interfere with the germ line.[103]

The above evidences show the continuing pressure within the European Parliament to have ethical restrictions on uses of embryonic or hybrid materials in the legislation. But the attempts failed and the ethically contested clauses were ultimately left out. Paradoxically, had the exclusions been incorporated into the legislation, the effect would have been to leave advanced therapies based on the use of the morally excluded tissues outside the reach of the regulatory controls on quality and safety standards introduced to safeguard the health of EU citizens.

The new Regulation on advanced therapy medicinal products aims at laying down: uniform technical standards on quality and safety of bioengineered products; centralized procedures for marketing authorisation through the EMEA;[104] and uniform procedures on post-authorization pharmaco-vigilance.[105] The ATR also creates a new European interdisciplinary advisory expert Committee on ATMPs, or 'Committee for Advanced Therapies',[106] responsible, *inter alia*, for preparing scientific expert opinions on the quality, safety and efficacy of each advanced therapy medicinal product for final approval by the EMEA,[107] and for consulting and liaising with the Committee for Medicinal Products for Human Use.[108]

Most of the dispositions of the ATR, which is a *lex specialis* to EU Directive 2001/83/EC, are mandatory and aim at harmonising technical standards on health and safety across Member States. They are therefore typical examples of the 'techno-regulation' model involving mandatory, uniform standards enforced through a regulator (the EMEA) as described in our matrix. For example, the ATR mandates Member States to ensure the traceability of the components of a medicinal product during the whole manufacturing process,[109] especially for products deriving from human tissue and cells;[110] it introduces prescriptions in on pharmacovigilance relating to follow-up of the efficacy, adverse reactions and risk management of these products;[111] it also introduces incentives for the small/medium sized enterprises. In its Annexes, moreover, the regulation introduces fixed and mandatory prescriptions regarding labelling, including most notably 'ethically' driven labelling as discussed above.[112]

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103 Ibid.
104 ATR, Charter 3.
105 Ibid., Chapter 5.
106 Ibid., Chapter 7.
107 Ibid., Article 8(2).
108 Ibid., Article 8(1), Article 8(3).
109 Ibid., Article 15.
110 Ibid., Article 14(3).
111 Ibid., Article 14.
112 Ibid., Annex II.

The second-order, flexible normative principles on consent and privacy regarding donation and procurement of tissues and cells contained in the EUCTD are imported into the ATR in Article 3. Similarly, on the previously ethically contested question of the centrality of altruism/non-payment in relation to sourced tissues and cells, the ATR follows the compromise-wording of the EUCTD. The ATR uses aspirational language enjoining – but falling short of requiring – voluntary and gratuitous donations on the grounds that this 'may' contribute to the quality and safety of the material itself.[113] The aspiration is further softened by its inclusion in the preamble only, with no counterpart mention in the binding part of the text. Thus, whilst the preamble states that '[a]s a matter of principle, human cells or tissues contained in advanced therapy medicinal products should be procured from voluntary and unpaid donation' and 'Member States should be urged to take all necessary steps to encourage a strong public and non-profit sector involvement in the procurement of human cells or tissues',[114] there is no obligation or corresponding enforcement procedure or penalty for Member States that opt to depart from the altruistic model. As regards payment for commercial trade in human tissue and cells, the ethical norms contained in the ATR conform to the normative open-ended model of regulation.

Finally, on the constitutionally sensitive and ethically contested question regarding the adoption of an EU-wide policy on controls relating to the use of human embryonic or animal cells on which European Member States are divided, the ATR follows the EUCTD approach, by avoiding any position. Notwithstanding the strength of a broad pan-European political spectrum combining primarily Christian Democrats and Green MEPs opposing the use of human embryos in research, the attempts to force moral exclusions in the EU legislative texts ultimately failed. Member States are left free to adopt restrictive rules reflecting national cultures[115] on 'the use of any specific type of human or animal cells, or the sale, supply or use of medicinal products containing, consisting of or derived from these cells'.[116]

The legal concession to the moral integrationists in Europe in the ATR comes in the form of a requirement regarding labelling. Following the precedent set over labelling of GMO products, Article 29 and Annex III of the Regulation imposes a strict obligation on labelling of ATMPs products, specially requiring that the label contain not only a description of the active substance(s) but a statement that 'This product contains cells of human/animal [as appropriate] origin *together with a 'short description of these cells or tissues and of their specific origin, including the species of animal in cases of nonhuman origin* [emphasis added]'. It is not difficult to anticipate a number of difficulties in specifying in a publicly accessible manner the precise nature and content of the sourced materials. This is no doubt an area in which the newly created advisory committee will

113 Ibid., Recital 15.
114 Ibid.
115 ATR, Recital 7.
116 Ibid., Article 28(3).

have a central role to play. The practical outcome, however, is a legal slide of the 'normative' dimensions of the model into the 'techno-regulation' model, as the ethically driven labelling requirements fall to be monitored and enforced by the central regulator.

§4. CONCLUSION

The above analysis shows that the EU deals with ethical and constitutional tensions in the regulation of morally contested new technologies through the adoption of 'mixed' forms of legislation which, we have suggested, may be mapped against an analytical matrix revealing a mix of evaluative and non-evaluative elements. The matrix distinguishes between technical standard-setting norms driven by medico-scientific problems relating to health and safety and overarching 'first order' fundamental norms incorporated from European human rights instruments and guiding the formulation of more specific 'second order' norms introducing flexible ethical restrictions on the use of the ethically contested technologies. Within the matrix, these norms range from compulsory to optional and their formulation from rigid to open-ended flexible wording, the substantive content of which has been left to the discretion of Member States.

Our analysis thus shows that whilst the original constitutional framework of the European Union points to 'techno-regulation as the favored mode of regulation, ethically motivated regulation has taken-off in the field of new biotechnologies and their application in biomedical contexts. EU health policy, whilst primarily focused on risk management and prevention in healthcare, to be achieved through health and safety value-free regulations, has had to respond to political pressure to situate the legislation within an ethical frame. This has been achieved through the incorporation of the largely open-ended and indeterminate norms contained in overlapping and disjointed EU human rights instruments which in turn guide the flexible and more specific ethical constraints contained in the legislative texts.

The controversy over the inclusion and control of the 'morally' contested technologies in the regulation of biotechnological therapies in Europe, therefore, shows the delicate and complex interface of the formally limiting constitutional framework of the European Union as regards respect for State autonomy as against the political reality of the forces seeking moral integration in Europe and representing Member States in the tri-partite institutional legal order, most notably the European Parliament. As the pace of advance in the biosciences quickens and novel and ethically contested applications emerge, the EU will continue to face fundamental challenges to the coherence and integrity of its legal architecture in its attempt to reconcile respect for ethical diversity and plurality with continuing political pressure for moral integration in Europe.