

EUROSTEM

AN ETHICAL FRAMEWORK FOR STEM CELL RESEARCH

This ethical framework is intended to be read as a complement to the many existing ethical frameworks concerned with human subject research, and not as a replacement for them. In our minds, an ethical framework is not a legislative proposal. It is intended to act as a reminder of the values that we all share and of the standards of ethical conduct to which we aspire.

INTRODUCTION

In considering and drafting this document, we are aware that we build on much excellent work and we acknowledge our indebtedness to those who have already grappled with these problems. We hope to explain and justify our proposals as far as is possible in a document that also aims to be brief and readable. We will start by noting that research, including stem cell research has a powerful moral base and imperative.

THE MORAL BASE OF STEM CELL RESEARCH

There is a powerful obligation to pursue, support and participate in scientific research. Two separate but complementary lines of argument lead to this conclusion.

Do no harm

First, it follows from one of the most powerful obligations that we have, the obligation not to harm others. Where our actions will, or may probably prevent serious harm then if we can, reasonably (given the balance of risk and burden to ourselves and benefit to others) we clearly should, act because to fail to do so is to accept responsibility for the harm that then occurs.¹ This is the strong side of a somewhat weaker, but still powerful duty of beneficence, our basic moral obligation to help other people in need. Most, if not all diseases create needs, in those who are affected, and in their relatives, friends and carers and indeed in society. Because medical research is a necessary component of relieving that need in many circumstances, furthering medical research becomes a moral obligation. This obligation is not limited to actual physical participation in research projects, but also involves supporting research in other ways, for instance economically, at the personal, corporate and societal levels and indeed politically.

Fairness

Second, the obligation also flows from an appeal to basic fairness. This is sometimes expressed as an appeal to the unfairness of being a “free-rider”. We all benefit from the existence of the social practice of medical research. Many of us would not be here if infant mortality had not been brought under control, or antibiotics had not been invented. Most of us will continue to benefit from these and other medical advances (and indeed other advances such as clean drinking water and sanitation). Since we accept these benefits, we have an obligation in justice to contribute to the social practice which produces them. We may argue that since we could not opt out of advances that were made prior to our becoming capable of

1. The arguments for, and the basis of this duty were set out in John Harris, *Violence & Responsibility* (London: Routledge & Kegan Paul, 1980).

autonomous decision making we are not obliged to contribute. But it may still be unfair to accept their benefits and implies also that we will forego the fruits of any future advances.² Few however are willing to do so, and even fewer really willing to forgo benefits that have been created through the sacrifices of others when their own hour of need arises!

The Moral Imperative For Research

We all benefit from living in a society, and, indeed, in a world in which serious scientific research is carried out and which utilizes the benefits of past research. It is both of benefit to patients and research subjects and in their interests to be in a society which pursues and actively accepts the benefits of research and where research and its fruits are given a high priority. We all also benefit from the knowledge that research is ongoing into diseases or conditions from which we do not currently suffer but to which we may succumb. It makes us feel more secure and gives us hope for the future, for ourselves and our descendants, and others for whom we care. If this is right, then I have a strong general interest that there be research, and in all well founded research; not excluding but not exclusively, research on me and on my condition or on conditions which are likely to affect me and mine. All such research is also of clear benefit to me. A narrow interpretation of the requirement that research be of benefit to the subject of the research is therefore perverse.³ This research has, of course, to respect all the generally agreed constraints on human subject research.

However, freedom of research is not unlimited. It has to be undertaken responsibly, within an accepted ethical framework, and in accordance with generally accepted moral principles. What these moral principles should include is the subject of this document.

CONTENTIOUS ISSUES IN STEM CELL RESEARCH

The Embryo

The most persistent differences in the debate about human stem cell research relate to the intractable question surrounding the moral status of the embryo. For all practical purposes, in the context of stem cell research, when we refer to the embryo we mean the early embryo. The continuum of opinion ranges from belief that the early embryo is merely a collection of cells to it being accorded the full status of a human being. This question has proved resistant to resolution through philosophical analysis or by scientific definitions. The moral status, or degrees of protection to be accorded to the embryo is constituted linguistically, culturally, scientifically, politically and through religious and secular beliefs. In order to protect the autonomy of each nation to decide their specific and particular approach to human stem cell research the principles invoked will generally involve an *issue of scope*.

Cell Nuclear Replacement

The issue of cell nuclear replacement (CNR) raises several ethical concerns. It is considered by some commentators that the creation of early embryos, sometimes referred to as blastocysts, for research purposes is a wrong in itself. However, each country must decide the limits of permissibility of research and hence the scope of protections and prohibitions. There is a question about the availability of oocytes. There may be pragmatic approaches to this,

2. Jonas, Hans, 'Philosophical Reflections on Experimenting with Human Subjects', in P.A. Freund (ed.). *Experimentation With Human Subjects*, (London: Allen & Unwin, 1972).

3. See, for example, John Harris 'The ethics of clinical research with cognitively impaired subjects,' *The Italian Journal of Neurological Sciences* **18** (1997) 9-15.

such as the donation of oocytes by a family member in the manner of organ donation. Another potentiality within future research may be that it becomes possible to make oocytes *in vitro* from human embryonic stem cells. However, the main argument advanced against CNR is that it will encourage reproductive cloning. This fear seems exaggerated. We should note that we can, and actually have in most countries succeeded in handling this version of the slippery slope argument by clear legislation.

Issue of Scope

The extent to which the embryo is to be protected, and the question of when, why and at what stages of embryonic development protections are required is part of ‘scope’ as it is understood in this document. This ethical framework is intended to apply to all, and any stem cell research whatever its scope. It is our hope and intention that it will be as applicable to jurisdictions which, for example, might permit research only on adult stem cells, or permit only non-destructive research on embryonic stem cells, as it is to those which permit such research only on cell lines created before a specified date, or, as in the UK, on cells from embryos before 14 days development.

The ability of all nations to support a joint approach to stem cell research through commitment to the principles set out in this document can be facilitated through the concept of scope. While human rights in one form or another command almost universal respect there will necessarily be arguments about scope. Scope concerns the range of individuals able to make moral claims and the precise nature of those claims. Arguments have always raged, for example over whether or not embryos and fetuses are included within the scope of “human persons” and over whether a right to life or the obligation to respect the sanctity of life permits war or capital punishment. These are questions of scope. Those disagreeing about such things do not usually disagree about the importance of the sanctity of human life or as to whether murder is the most serious of moral offences. They tend to disagree about whether or not a particular case is in fact a case of murder or whether the individual killed was a person in the relevant sense.

Important as questions of scope are we judge it important to avoid any attempt to resolve them, partly because the disputes about scope are about as intractable as disputes can be and partly because we do not need to resolve them. We frame our principles in the hope that they will command wide if not universal agreement, knowing that the scope of the principles will continue to be debated and aware that toleration requires that we permit societies and to some extent individuals to differ about the scope of the principles they accept.⁴

4. For the record we note that recent legal decisions of the European Court of Human Rights confirm (European Court of Human Rights, *Case of Vo v. France* (Application no. 53924/00), Judgement, Strasbourg, 8th July 2004) that the unborn are beyond the scope of principles such as those with which we are concerned.

AN ETHICAL FRAMEWORK FOR STEM CELL RESEARCH

Preamble

The development of a European framework for stem cell research is challenging for a number of reasons. It is complicated primarily because of the differences between regulatory and legislative positions, or lack of regulation, in the countries involved. It is further complicated by what may appear to be inconsistent legislation within countries which permit abortion and IVF treatment but ban research on early embryos. This lack of consensus is largely grounded in conflicting views of the moral status of the embryo, but may also reflect a demarcation of what are understood to be legitimate areas for statutory intervention. The pursuit of fertility treatment and the requirement of abortion facilities are widely considered to be choices within the domain of individuals.

It cannot be expected that legislation or regulation always be philosophically consistent as it is not merely moral considerations which drive policy. Furthermore, legislative and regulatory frameworks, where they exist, have their origins in, and are subject to, historical, political and cultural particularities. However, this does create tensions within, and between countries as they try to balance the competing requirements of freedom of research, academic autonomy and the duty of governments to best serve the health needs, and other basic rights of their citizens.

The challenges involved in creating an ethical framework for stem cell research within the nations of the European Union reflect the cultural diversity and the religious and political pluralism that exists within our nations. We have a powerful interest in promoting the values enshrined in the *Charter of Fundamental Rights of the European Union*. As a community of nations we have a clear joint interest in pursuing stem cell research. Our interests lie in continuing to support freedom of research, benefiting from the fruits of that research, and refraining from imposing onerous conditions on countries which endorse embryo research, or from disadvantaging countries which have restrictive conditions regarding embryo research. These interests include financial considerations in terms of novel scientific application in the hope that we may better protect the health of our populations through effective treatment of some of the most debilitating and costly diseases and conditions. We have a joint interest in the responsible pursuit of scientific endeavor which would be facilitated by working together through encouraging cross-nation multi-centre research. We have a combined interest in being competitive within the international market, and this is best pursued jointly, within an ethical framework, and through open, collaborative ventures.

Regarding the Principle of Respect for Persons

Respect for persons is widely regarded as the fundamental basis of any ethics involving human beings. We share the assumption of our society and indeed most if not all others that persons have the highest moral importance or value. The philosophical literature shows that this assumption can be explained and defended in a number of ways. Here, we need only note and endorse the wide acceptance of this principle by most religions and cultures. The term “respect for persons” encapsulates this ‘ultimate’ moral importance and attempts to give it content – to explain just what those who accept the moral importance of persons are committed to in concrete terms. Respect for persons understood as a moral principle sets out the ways in which it is appropriate to behave towards those who matter morally. Respect for persons then not only describes the outcome – treating others in morally appropriate ways, but also points to the origin of this obligation in the ultimate or supreme moral value of individuals. In regard to stem cell

research it requires us to be mindful of persons who might benefit both directly and indirectly from the fruits of this research. And, of course, those who regard the early embryo as protected by the *Principle of Respect for Persons* will here include such embryos among the class of beings to be protected.

Respect for persons which has long inspired a major line of thought in moral philosophy requires us to acknowledge the dignity and value of other persons and to treat them as ends in themselves and not merely instrumentally as means to ends or objectives chosen by others. Respect for persons has two distinct dimensions:

1. Respect for autonomy.
2. Concern for welfare of the subject.

These twin dimensions illuminate the stem cell debate in several ways. The respect for autonomy is relevant to the relationship between science and the public by way of being a reminder of the importance of academic and scientific autonomy and the fruits that this autonomy has provided for the welfare of all. It guides the relationship between researchers and research subjects; it protects gamete donors in the form of the requirement of informed consent which stems from respect for autonomy. It accords with the *Principle of Toleration and Pluralism*, in that the value of autonomy is expressed as the ability to choose, and have the freedom to choose between competing conceptions of how to live and, indeed, of why we do so. Concern for welfare complements autonomy in that it provides the conditions in which autonomy can flourish. Stem cell research seeks to benefit the welfare of those directly and indirectly affected with medical conditions which constrain autonomous life. The increase in knowledge and the potential amelioration of disease will contribute greatly to the autonomy and welfare of all thereby upholding the *Principle of Respect for Persons*.

The scope of this principle can, of course, be narrowed or widened depending on decisions as to what is to count as a person for these purposes.

Regarding the Principle of Equity in Stem Cell Research

The principle of equity in stem cell research holds that humans are born equal; they are entitled to freedom from discrimination and equality of opportunity to flourish; stem cell research and therapy may not be used to limit that equality.

It is important to stress that a commitment to equality as a moral and political ideal does not involve any claim that people are, or should be “the same,” except with respect to their rights, or interests, or with respect to their moral claims. Jean Jacques Rousseau pointed out that the notion of equality may have different meanings. In his *Du Contract Social*, we read:

*instead of destroying natural inequality, the fundamental covenant substitutes a moral and legitimate equality for the physical inequality that nature may have set up among men, and those who may be unequal in strength or intelligence become equal by convention and legal right.*⁵

This conception of equality also finds expression in ideas of human dignity. In Kantian ethics this principle demands that an individual should never be thought of merely as a means but always also as an end. The idea of the equal standing of each person, the idea that each is entitled to the same concern, respect and protection as is accorded to any; in Bentham's formulation of the idea, that each is to count for one and none for more than one, we have another but rather different appeal to human dignity. Human dignity is on this view expressed in terms of equal standing in the human community and in equal respect for rights and interests. Bentham's phrase is tellingly apposite, containing as it does two ideas. The first is the idea of counting equally - numerical counting. If one person counts for one then two count for two and so on. This idea shows us why we always have a moral reason to save more lives rather than fewer, because each life matters equally. Bentham's second idea contains the thought that people not only matter numerically, count for one, but that they also count in a more absolute and existential sense – they *count for something*, in short they *matter*, they count because they have equal dignity and standing. The principle of equity then protects human dignity and prohibits unfair discrimination. In the context of stem cell research it reminds us that both in its methods and its applications stem cell research must treat people as equals, with respect and avoid unfair discrimination.

Regarding the Principle of Toleration and Pluralism

There are many good reasons for supporting toleration as a guiding ideal, particularly within bioethics. It indicates a respect for the autonomy of states and individuals; it promotes the sense of humility required to refrain from imposing one's own judgments and beliefs on others; and it incorporates the virtues of cooperation and goodwill generally required for human flourishing. Much has been made of the perceived 'paradox of toleration', the belief that this ideal insists that we tolerate the intolerable. We consider the distinction between first order judgments and second order moral commitments. The former are identified by responses and judgments to particular actions and attitudes, for example, research on human early embryos. The latter incorporates a determination to promote a higher ideal. One which attempts to raise communities above the particular and toward rational universal principles such as respect for autonomy and recognition of cultural diversity. Given the pluralism of the European community, the second order moral commitment must prevail; principle outweighing particularity.

Regarding the Principle of Solidarity

This principle promotes the development of humanity through the spirit of cooperation. This principle is particularly important precisely because of the diversity and inconsistency of regulatory and legislative frameworks, or the lack of such frameworks, and the cultural, political and historical positions that this diversity illustrates. This principle is connected to the *Principle of Toleration* in that it demands that we rise above particular differences, even intractable differences, to promote the betterment and development of mankind. This would

5. Rousseau, J.J., *Du Contract social, ou Principes du droit politique* (Amsterdam: Chez Rey MM, 1972) Book 1, Chapter IX, translated from French by Simona Giordano and John Sulston. In elaborating this principle of equity, we have drawn on John Harris & John Sulston 'Genetic Equity' *Nature Reviews Genetics* 5 (October, 2004) 796-800.

encourage us to put in place regulation and legislation that encourage cooperation. For example, it could be a condition of any license granted that cell lines derived from early human embryos be made publicly accessible for a nominal fee to academic researchers.⁶ Commitment to the *Principle of Solidarity* will engender a commitment to the public funding of stem cell research and therefore widespread access to the results of research. It will encourage multi-centre research whereby stem cell researchers working within less liberal regulatory systems could still be involved in aspects of the research, for example, through the importation of cell lines. Instead of attempting the lengthy and fraught task of attempting legislative and regulatory harmonization, we should rather encourage research communities, supported by joint funding ventures, which help to protect the right to freedom of research and academic autonomy whilst maintaining each countries particular moral sensibilities or legislative history. These principles are chosen to guide and unite all relevant and interested parties in the field of stem cell research. The purpose of stem cell research itself, however, is grounded in the *Principle of Respect for Persons*.

Regarding the Principle of Informed Consent

Informed consent is a dimension of respect for persons in that it is through consenting to things that affect us that we make those things consistent with our own values. When we consent to what others propose we make their ends and objectives part of our own plans; so far from being merely the instruments of others we incorporate their plans and objectives into our own scheme of things and make them in that sense our own. That is why respect for persons precludes the non-consensual use of others merely for our own benefit, and explains why their consent to what we propose transforms them from mere tools of ours into self-regulating, autonomous beings whose chosen path we facilitate. Respect for persons recognises that the sense of identity that others have, their goals and beliefs are important to them, and must be respected by us.

Regarding the Principle of Beneficence

The *Principle of Beneficence* is the dictum to do good wherever possible. To be a guiding principle it depends largely on definitions of the good. As we noted in the introduction, it can be agreed that people are treated in a beneficial way through efforts which are made to ensure the well-being of persons, in particular, persons in need. The *Principle of Beneficence* in terms of scientific research and medical progress has as its goal the protection of our fellow citizens and the promotion of health and the advancement of welfare systems. This principle is relevant to stem cell research in that the goal is to directly benefit persons in need. In the case of scientific research in general, the benefit to society at large results from the improvement of knowledge in general and the development of new techniques and therapies to improve human well-being. Benefits have always to be weighed against risks.

Regarding the Principle of Wide Availability

In accordance with the *Principle of Solidarity* we would encourage the public funding of stem cell research, and support for the *Principle of Wide Availability* to the results of publicly funded stem cell research. This follows the model set by The Human Genome Project. Open access publishing permits free access to papers, for copy distribution and display purposes, subject to proper attribution of authorship. This would lend assistance to the trend that important medical research in the future will be openly accessible leading to the acceleration

6. This is currently the case in the UK under the HFEA regulations.

and growth of progress and knowledge, improved sharing of results and ultimately for the treatment of patients.

Stem cell research promises new knowledge of, and insight into the nature and mechanisms of disease, and the building blocks of life itself. This research is of such fundamental importance that it demands the widest possible dissemination of its results.

Regarding the Principles of Privacy, Confidentiality, and Control of Misuse of Information

The *Principles of Privacy, Confidentiality, and Control of Misuse of Information* stem directly from the *Principle of Respect for Persons* and are related to the *Principle of Informed Consent*. These principles are widely accepted in the area of biomedicine and genetics. Stem cell research involves access to medical and genetic data of the persons involved, for example, through the banking of stem cell lines, their distribution to other universities and research groups, and their use for different research purposes over time. Concerns have been raised about how these stem cells, and hence the medical and genetic information they contain, will be used and by whom. Persons, as autonomous beings, have a powerful interest in determining which personal medical information is processed, by whom and for which purposes. Therefore, any stem cell research should be carried out on the basis of anonymized data, or, when this is incompatible with the research or patient safety, such research must be carried out with respect for privacy of the persons concerned and the confidentiality of their personal data. Personal information obtained through such research should be used only for the objectives for which the person involved has consented, with possible exceptions that are in accordance with national law.

But because of the ease with which genetic information can be obtained from almost any sample of human tissue which contains cells including saliva, it is impossible even with goodwill to guarantee privacy and confidentiality.

Therefore, being aware of the impossibility to guarantee full respect for privacy and confidentiality, we recommend that strict professional and legal measures⁷ should be taken not to prohibit the obtaining of genetic information, because that is practically impossible, but to identify clearly acts that constitute misuse, and impose severe legal sanctions for misuse. This we call the *Principle of Control of Misuse of Information*.

Regarding Responsible Partnering: the complementary roles of public and private investment

Complementary to the role of public investment, private investment is an essential part of ongoing work concerning the understanding of stem cells and ultimately of obtaining benefits from this research. In accordance with the principles set out, particularly the *Principle of Wide Availability*, we encourage governments to adopt regulations that facilitate the transfer and translation of our understanding of stem cells, particularly between the public and private sectors and including across national borders. Equally, in accordance with the general need for public transparency, we encourage companies and universities to adopt the highest standards in respect of their management, organization and the external scrutiny of internal and joint research

7. Human Genetics Commission (UK), *Inside Information – Balancing Interests in the Use of Personal Genetic Data* (London: Department of Health, 2002).

8. Responsible Partnering, developed jointly by the European University Association, the European Association for Research and Technology Organisations, the European Industrial Research Management Association and ProTon Europe funded by the European Commission, sets out suitable standards.

Regarding the Principles of Promotion of Research and Protection of Individual Researchers

Promotion of Research

The promotion of research across Europe is a fundamental objective of the European Union and therefore funding should make possible research and collaboration and co-operation between researchers from different member states without fear of discrimination.

Protection of Individual Researchers

Because of differences in national legislation, collaborative work in the EU is fraught with dangers. For example, work done in one country which is forbidden in another exposes those undertaking this work to the risk of criminal liability for their involvement in this work. This also potentially excludes researchers from funding.

Recommendations concerning *Promotion of Research and Protection of Individual Researchers*

- To the extent that national laws prevent such co-operation and collaboration, we recommend that nation states and the European Commission work actively to find solutions for this problem.
- The solutions cannot be the responsibility of individual researchers. No one working in the EU should be punished or rendered liable to prosecution, restriction or discrimination if they participate in research so long as the research is undertaken in a country permitting such research.
- European research should be funded in a way that does not discriminate between individual states and researchers in the EU. This means that individual researchers should not be disadvantaged or be the object of discrimination by reason of their participation in research.
- The funding policy of the EU should be aligned and made consistent with the above principles and should not disadvantage researchers in any member states.