

# Advanced Workshop on Embryo Research

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**European Federation of Biotechnology Task Group on Public Perceptions of Biotechnology** is an independent European expert group with the aim to encourage the social debate and dialogue on issues on modern biotechnology. ([www.efbweb.org](http://www.efbweb.org))

**Genetic Interest Group** is an alliance of support groups for people affected by genetic disorders. It is a registered charity in the UK (No 803424)

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## Introduction

This workshop brought together a diverse group of experts – embryologists, geneticists, representatives of patient groups, lawyers, ethicists, science communicators and others to look at the potential that embryonic stem cells have for advancing our understanding of fundamental biological process in serious human diseases and their prevention, treatment or even cure and the factors that may permit or prevent the exploration and/or the realisation of this potential.

The workshop was convened by the European Federation of Biotechnology Task Group on the Public Perceptions of Biotechnology and the Genetic Interest Group (the UK alliance

of support groups for families with genetic disorders). It was funded by the European Commission (DG Research). Participants were invited to attend on the basis that, although a report would be produced their remarks would not be attributable (the Chatham House Rule). This was to encourage a full and frank exchange of ideas and opinions. This objective was achieved. Hopefully this report captures something of the flavour of the meeting and records the main aspects of the discussion, although inevitably the process of writing it will omit some ideas and highlight others in ways that other participants, had they been responsible, would have chosen to do differently.

### 1 – Ethical and Moral Dilemmas in using Human Embryos in Research

Recent developments in research have indicated that human embryonic stem cells have enormous potential for adding to our knowledge of and relieving suffering from, many serious human diseases. Yet the use of human embryos in research is highly controversial and raises complex ethical questions. For some, the fact that the creation of embryonic stem cell lines for research necessarily requires the destruction of pre-implantation human embryos makes this line of research unethical. For those who do not take this absolute view, the question that must be addressed is “Does the end justify the means”? If so, ought limits to be placed on what is permissible and how can a proper framework be constructed that will permit research but prevent abuse?

The use of animals in research may help to frame the question. Moral questions about animal based research have encouraged scientists to seek alternatives where possible, with a goal of reducing and refining the use made of laboratory animals. However alternatives to animals are normally only introduced when they have been demonstrated as being equally scientifically valid. Where there is a scientific consensus that animal use is necessary and justifiable, moral questions are not normally allowed to over-ride this view. Central to the arguments for this justification is the seriousness of the purpose of the research and of the questions it is intended to address. In the case of human embryonic stem cells it seems likely too that, given prevailing scientific opinion as to the hoped for:- benefits, moral objections are unlikely to achieve ascendancy. If the end are judged by society to be important enough, then the means to achieve them are justified.

This is not to give carte blanche to all forms of embryo research. Just as with the use of animals some research is prevented even though it may be of great benefit (for example the use of Great Apes in the UK) so some embryo research will be felt to be

inappropriate. The problem is to define a set of criteria for determining where the boundary should be drawn.

Discussion of the way in which we should regard embryos is often couched in terms of “respect for life” and the “sanctity of life”. Although both phrases are used as if they were interchangeable, in fact they have different connotations. “Sanctity of life” originates from a religious belief that affords the embryo absolute protection because it has a human soul. “Respect for life” on the other hand, has a more secular derivation from the recognition of the reality of the belief that those of a religious nature hold, even if the beliefs themselves are not shared. This creates the need for a public compromise to be formulated that will permit stem cell research to proceed. But this should be more than a compromise between “absolutists” and “pragmatists” with the line drawn at the point where the two have fought themselves to a standstill.

“Respect” in moral philosophy often derives from Kant’s use of the word, when he talked of “respect” for person as ends in themselves? In German the word is “Achtung”, which carries with it the notion of wariness, much as a wise person “respects” a live electrical wire.

Something of this “Achtung” quality is lost if the pre-implantation embryo is simply a laboratory artifact. But it is also difficult to sustain that the early embryo “a bundle of 16 or so cells” requires as much “Achtung” as a fully formed baby.

Contrast this notion of wariness with the idea of the “sanctity of life”. The notion of “life” of being alive arises from more than the completion of a series of complex biological processes. “Life” is also defined in our everyday experience from the sort of responses that occur when one living thing recognises another. So the “sanctity of life” is compromised when one

living thing fails to recognise and respond to another appropriately – in personal and subjective terms, not just in biological or objective ones. Seeing the embryo either as a laboratory artefact or as a member of the human race is the context in which the notion of “sanctity” acquires meaning.

The pre-implantation embryo’s potential evokes the “Achtung” response notwithstanding the realisation that, even in the most favourable of circumstances only a minority of embryos will fulfil their potential. We do not use resources to preserve these lost lives in the way that neo-natal intensive care units try to save very premature babies. To do so would seem disproportionate both on biological grounds, as the majority of those embryos are fatally flawed anyway and on existential grounds. For most people, thinking of the pre-implantation embryo as “you” not “it” is difficult, if not impossible. The transition from the third to the second person seems to be a gradual one.

For many people the difficulty lies in defining the acceptable middle ground. Neither end of the spectrum is a comfortable

place to be. Resolving this difficulty may be helped by the Paul Ricoeur’s notion of “practical wisdom”. Listening to both sides suggests a succession of qualitatively different rights, running from the “right not to suffer” through the “right to protection” to the “right to respect” once there are intimations of an exchange, no matter how asymmetrical between the fetus and its mother.

The notion of an exchange reflects the intuitive and traditional views held by many cultures – “quickenings” and the notion of “ensoulment”. It implies that the embryo occupies an intermediary position between things and people, with greater certainty about its moral status becoming possible as thresholds are crossed as it develops.

The use of embryos in research evokes conflicting moral concerns regarding the goals of the research and the means to achieve them. Against this background a degree of reticence about our behavioural towards embryos seems appropriate.

## 2 – Biological Possibilities and Current Biomedical Research

The potential that embryonic stem cells offered for understanding complex biological processes was first highlighted by Patrick Steptoe in the late 1960s. It is not a recent phenomenon. Work using animal models has led to the potential for investigating human disease that is now being appreciated once again.

Study of teratocarcinomas (tumours which grow to contain many differentiated cell types and which can be seen to be like a “disorganised embryo” in which it is sometimes possible to recognise discrete structures such as a limb, nervous tissue *etc*) gave rise to a realisation that embryonic stem cells and the undifferentiated tumour cells were biologically very similar. For example a cell from a mouse teratocarcinoma will, if transplanted into a mouse embryo, take part in normal embryonic development and give rise to a chimeric mouse.

Stem cells in the early blastocyst will, under normal circumstances develop into the embryo. If they are extracted they can be made to proliferate and form embryonic stem cell lines, with the potential to differentiate into many different types of mature cell.

Early experiments to produce embryonic stem cell lines were very inefficient with successful lines resulting in only about 10-15% of cases. Improved techniques now produce a success rate in the order of 50%, reducing the number of embryos that have to be sacrificed substantially.

In mice it is possible to verify that cell lines established are stem cells by transplanting them into embryos and observing their participation in normal development. This would be unethical in

humans so proof of the establishment of an immortal stem cell line is obtained using a surrogate marker – the activity of the enzyme telomerase – which disappears at birth. (Tumour cells also show telomerase activity)

Human embryonic stem cells are pluripotent. They can differentiate into any type of cell normally found in the human body. The issue for research is to drive this differentiation in the desired direction, avoiding uncontrolled proliferation of unwanted cell types.

Work with mouse embryonic stem cell lines has produced differentiated cardiomyocytes – beating heart muscle cells. In rats transplanted dopamine producing cells derived from embryonic stem cells have restored neural functions. Myelin production has also been possible using transplanted embryonic stem cells. This has obvious possibilities for transfer to humans with Multiple Sclerosis, but great care must be taken to avoid extrapolating from animal models to humans too quickly. Nevertheless, these and other developments in animal models indicate great potential and there has been a rapid expansion of research activity using existing human embryonic stem cell lines. Early reports seem to mirror the potential benefits found in mice.

In the USA the FDA gave approval for nerve cells derived from teratocarcinoma stem cells to be transplanted into the brains of 11 stroke patients in 1998. (NB Some felt this experiment to be premature because of the tumourigenic potential of the transplanted cells). In 1999 the transplant cells were still evident. By 2000 no patients had developed tumours and 6 of the original 11 were showing signs of improvement. This year (2001) approval was given for a phase II trial to be commenced.

In the longer term there are significant potential gains for human health to be realised from this type of research. Areas where this new knowledge may be applied include:

Now	Drug testing for toxicity/efficacy
Mid term (5-10 years)	Transplantation <ul style="list-style-type: none"> <li>• Dopaminergic/cholinergic receptors</li> <li>• Bone marrow/haemopoetic cells</li> <li>• Muscle</li> <li>• Pancreas</li> <li>• Endothelial cells</li> <li>• Cardiomyocytes</li> <li>• Glial and neural cells</li> </ul>
Long Term (10+ years)	Transplantation <ul style="list-style-type: none"> <li>• Cells of liver, kidney, thymus <i>etc</i></li> </ul>

Clearly this will not be straightforward and a number of major obstacles remain to be overcome before this potential can be realised. These centre on the difficulties of obtaining pure cells for transplantation and controlling their differentiation satisfactorily. Tissue rejection will also need to be prevented, or be reduced by appropriate use of drugs and better techniques of tissue matching.

One issue which will need to be resolved is the number of different immortal cell lines that will need to be established to offer the prospect of a reasonable tissue match for people who need a transplant. Current estimates suggest that 2-300 may be sufficient, although the number may vary according to the nature of the recipient organ. (The brain, for example has low immunogenic activity). Homogeneous populations may also need fewer lines than more heterogeneous ones.

With efficiency of establishing cell lines now reaching 50% the number of embryos required may not be unacceptably large.

Associated with the use of stem cells lines derived from spare embryos is the possibility of creating embryos using cell nuclear replacement and isolating stem cells whose nuclear DNA is identical with the nuclear donor. Of course the mitochondrial DNA is that of the donor egg, creating a potential immune response and at the present the efficiency is very low. Given the low availability of eggs from all sources the cost justification of this research at present must be carefully scrutinised.

One way of reducing immune responses and hence the level of immunosuppressive medication required may be by genetically modifying the stem cells, but transferability of the techniques to humans is by no means certain and further research needs to be carried out. Whether or not this is possible may depend on the public perception of its acceptability as much as its biological feasibility.

Adult stem cells are cited as an alternative to embryonic stem cells and indeed recent research has shown that they are not restricted to their own "niche" in the body but are capable of showing a surprising degree of plasticity. Adult stem cells are to be found in skin, hair follicles, natural cells and bone marrow (the most likely source for future development).

Clearly the use of adult stem cells is an option which ought to be developed fully, but they create problems of their own which would make it premature to drop work on embryonic stem cells at this stage. Amongst these problems is their accessibility. They are hard to find and few in number (less than 1 in 100 million). Maintaining their growth and differentiation capacity is difficult and may raise questions of safety that will need to be addressed.

Compared with adult stem cells we know now that embryonic stem cells are accessible (with a 50% efficiency of isolation). They are pluripotent and can differentiate into all types of cell found in the body. Animal experiments show they can form functional tissues after transplant and clinical trials show they have not found tumours and are still working more than 2 years after transplanted.

Among the diseases which may be treated and possibly even cured by the use of therapies derived from stem cells are :-

- Stroke
- Parkinson's Disease
- Multiple Sclerosis
- Diabetes
- Heart Failure
- Spinal Cord Injury
- Vascular Disease

(All diseases where one or a few cell types either disappear or fail to function)

Before this can happen a number of problems need to be solved, including the development of a satisfactory feeder cell substrate for growing stem cell lines on that regulatory authorities are satisfied does not engender health hazards and trying to work out why "spare" embryos have a higher efficiency than created ones as sources of stem cell lines.

All these issues will not be resolvable in mouse models alone because there are significant biological difference between mice and humans making extrapolation difficult. Eventually it will be necessary to address these questions in human derived cells.

The potential benefits of this research have attracted commercial investment and stem cell lines are currently held by biotechnology companies. This has necessitate the negotiation of material transfer agreements but this has not proved a hindrance to scientific research in practice. Of course there is the possibility of failure. The research may not deliver. Commercial agreements should not prevent the publication of all results, positive and negative if academic freedom is to be preserved.

At the moment it is clear that there is great potential for benefiting human health emerging from the study of embryonic stem cells. Realising it will require sustained research and a regulatory framework that is sufficiently flexible to realise this (if it turns out to be biologically possible to do so) whilst at the same time preventing abuse or the conduct of research which is unethical or unsafe.

### 3 – An ethical framework for decision making

The debate about the moment at which life begins is not one which is resolvable by reference to objective criteria. It is rather a function of personal belief and ethical arguments are used to justify a variety of positions as to when the defining moment occurs (if indeed there is a defining moment). In order to create a framework for decision making it can be seen to be helpful if the parameters of the issue are articulated so people can use them to frame their own position on the issue.

For conservative thinkers the embryo is a human being from the moment of conception, worthy of all the rights and protections afforded to human beings. Destruction of the embryo is murder and the innocence and vulnerability of embryos are a compounding factor. At the other end of the spectrum is the view that the embryo is just a “thing”. It has no self awareness and it doesn’t satisfy the conditions necessary for person-hood, so it should not be afforded any more respect than any other human material.

Between the extremes is the view that the potential for personhood requires increasing protection as comes closer to being realised. Recognition of this position has implications for public policy and requires the clear definition of levels of protection to be adopted for embryos used in research. In the UK, for example, the view has been taken following public consultation procedures that embryo based research is necessary and indeed desirable for specific purposes defined by law. Elsewhere in the European Union states have taken a fundamentally different view on the morality of using human embryos in medical research. Even within States groups can differ radically from one another, raising questions about the reality of a collective national morality. Is this just a balance of opinion, influenced by when and where we live – the cultural, legal, social, political and religious background of our society or are models transportable across national boundaries into different contexts?

Existing regulations offer a (greater or lesser degree) of protection to embryos. Developments in embryonic stem cell research offer a challenge to the assumptions that regulation is based on, in that it holds out the promise of benefits to tens of thousands of currently sick people. The question is whether this potential is sufficient to challenge existing frameworks and whether these are flexible enough to respond.

A particular challenge seems to be posed by the possibility of creating embryos by cell nuclear replacement. Some societies (for example the UK) allow the creation of embryos for research, whilst others (eg Netherlands) only permit the use of spare embryos. The Council of Europe’s Bioethics Convention prohibits the creation of embryos but allows signatories to opt out of the prohibition. It is arguable that the creation of embryos for research is more acceptable, not less, than the use of spare embryos because the intention is different from the start and there is never a possibility that they will be implanted.

The creation of embryos invokes the possibility of reproductive cloning. This arises because there appears to be an innate public suspicion that scientists will be unable to resist the temptation

to implant – that there is a “slippery slope” which we will rush headlong down.

Arguments of this type ignore the fact that “slippery slopes” exist in many guises and legislators and regulators have been able to install barriers (in most cases successfully) at the appropriate point, allowing progress to reach the point where it remains acceptable, but stopping development before it crosses the line.

Given the potential of adult stem cells, is it ethical to continue using embryonic ones? Scientific arguments stress the latter’s potentially greater flexibility and the fact that they may be a stepping stone to greater understanding of adult stem cell biology. Logically it seems inappropriate to stop one productive line of research just because another seems promising. This would appear to do a disservice to potential beneficiaries from the outcomes of embryonic stem cell research.

As has been stated, there is an considerable divergence of opinion as to the acceptability of embryonic stem cell research in Europe. If the research delivers safe and effective treatments for serious diseases, should those countries which regard the research as unethical permit their citizens to benefit.

If access is denied, based on the view of the embryo, it will automatically raise the issue of the reality of the existence of a “national morality” and the rights of those who do not subscribe to the viewpoint articulated to be denied the possibility of relief from their suffering. In a free market the right of citizens to travel to receive health care is acknowledged. It might appear hypocritical to permit those able to afford it the opportunity to purchase effective treatments denied to fellow citizens in equal need but who happened to be materially poor.

Of course the realisation of benefits may result in states re-evaluating existing restrictions, as is happening in France and Germany or it may allow the results of the research to be used whilst maintaining a ban on research itself. This would raise accusations of hypocrisy that would be hard to refute.

Confusion over national morality has resulted in fudges, often creating worse problems than the ones they attempted to solve. For example, in the USA the Clinton presidency allowed embryonic stem cell research but it did not allow federal funds to be used to pursue it. Now President Bush allows stem cell research, but only on embryonic cell lines developed before 9.00am on 9th August 2001 (Eastern Standard Time). It is inevitable that more and better lines will be developed. The imposition of an arbitrary deadline might force American researchers to develop treatments that will be derived from lower quality starting points if this ban remains in force.

Realistically it seems unlikely that a satisfactory international consensus on the acceptability of using embryonic stem cells in biomedical research will emerge. Most regulatory frameworks include an element of hypocrisy – but about different things (for example the possibility of using Great Apes in research). The need to draw a line between the do-able and the unacceptable may not be based on logic, but on other factors such as the need

to reassure the public that the risk and their views on the risks are being taken into account and so maintain the legitimacy of research.

A pragmatic solution to the political problem of inconsistency may provide a way forward.

This pragmatic approach will need to recognise that a “national moral identity” is a difficult concept to sustain and the

differences within populations may be at least as great as those between them. Drawing lines, as for example in the case of cloning where the distinction between therapeutic and reproductive uses is made may provide opportunities for progress, even though both routes depend on a common technology at first. Finally, there may be a need to develop “generosity with each others hypocrisy” and avoid too quick a rush either to condemnation or to the imposition of uniformity where, in reality none exists and it is impossible to manufacture.

#### 4 – A Regulatory Framework – the UK Model

The development of a framework for regulating embryonic stem cell research can be based on the assumption that this is simply an extension of existing controls on embryo research, but the question needs to be asked if this is logical or is stem cell research significantly different in character – perhaps because embryos can be used for purposes unconnected with fertility and reproduction.

Any regulatory framework has to fulfil a number of purposes if it is to be deemed successful. These include the maintenance of public confidence, exercising control of the research to those areas which are compatible with social and ethical norms. The process of regulation must be carried out by a body that is and is seen to be, competent and legitimate.

Clearly the point at which standards are set will vary between jurisdictions but the process whereby decisions are arrived at is, in itself valuable. In the UK this has permitted the maintenance of a measure of flexibility within a legally established framework within which those wishing to undertake embryo research are able to proceed subject to the issue of a license, which will have conditions attached and provided they have been able to convince the regulatory authority (the HFEA) that the use of embryo is justified and the work proposed is necessary or desirable. This offers a degree of protection against the frivolous use of embryos. As does the requirement that the researcher obtain informed consent from the donor of the embryo for research uses.

The UK’s original legislation allowing embryo research for defined purposes has been challenged by the development in stem cell research and Cell Nuclear Replacement, both of which create new opportunities and potentially raise new anxieties. In the light of these developments and following extensive public consultation the law was amended to permit new uses (not new technologies – these were already developed prior to the legislation) Consultation focussed on the acceptability of using embryos for research purposes not associated closely with reproduction and conversely the justification for withholding the application of technologies already permitted in a reproductive context to the resolution of problems associated with diseases that were possibly more devastating in their impact than infertility.

Nor must the issues be taken out of proportion. As knowledge advances, so the number of embryos needed may be small once sufficient stem cell lines are established capable of meeting the need.

Once stem cell lines are established the emphasis shifts, as it is no longer a question of embryo research and the focus of regulation will need to be move to questions such as use, storage and safety of the lines. Once the capacity to develop into individuals has been lost the question must be asked if we need to regulate research in the same way – and does this shift undermine existing controls on embryo research?

An example of the issues that might be addressed is the question of consent. Embryo research requires informed consent of the donor. To what extent is this necessary when looking at research proposals using immortal cell lines? Clearly there are a number of major difficulties if this was deemed to be the case – including the practical problems of obtaining consent, the complexity of the information that would need to be communicated and the fact that potential future uses are not known at the time the cell line is established. Rolling the existing system forward to cover embryonic stem cell lines is not an option because it is unworkable.

In creating a framework it is essential to be clear about what in fact we wish to regulate and clarify distinctions between embryos and embryonic stem cell lines.

In the case of the latter regulation might concentrate on issues such as record keeping and quality controls, on safety issues (such as the feeder cell cultures used) and on the establishment of clear audit trails to check on the source, distribution and uses of particular cell lines. International aspects to regulations would also be important, with appreciation given to the issues raised by the import and export of cell lines around the globe (and giving due respect for pluralism and different ethical codes)

It is clear that the science will continue to develop. There is a need to manage the regulatory process to ensure the continuing compatibility of scientific potential and societal norms, exercising wisdom in the placing of boundaries at the appropriate point on those “slippery slopes” that may exist

In forming regulations to control embryonic stem cell research and development it seems sensible to lay down a few broad principles rather than seeking to micro-manage the future biological possibilities. Broad drafting will go some way to future proofing any legislation, giving regulators the freedom to fulfil their remit and avoiding sudden changes of policy

resulting from the re-visiting of existing frameworks in the light of new knowledge, Arms length arrangements can be seen to reduce the politicization of the issue, creating and sustaining public confidence in the appropriateness and the independence of the regulatory framework once it is established.

## 5 – The Role of Patient Organisations

Advances in biological understanding of the potential benefits of treatments that might be derived from the use of embryonic stem cells led to pressure to amend legislation and allow research to proceed. Central to this pressure in the UK was a coalition of patient groups representing those who are living with a wide range of chronic serious and often threatening disorders and for whom there is no currently available alternative treatment.

The legislative process begun in the UK Parliament following the publication of a report by the Government Chief Medical Officer. This highlighted the broad consensus from clinicians, scientists, industry and patient organisations that this was a very promising research area that should be encouraged if the benefits were to be realised.

However it was recognised that it is a sensitive issue and that many people hold views that are absolutely opposed to this type of research on religious or moral grounds.

The UK parliamentary process is an oppositional one. The Government decided to allow a free vote (*ie* not on party political lines) on the issue and once the draft regulations were introduced to Parliament attempts were made by both “camps” to persuade MPs and Lords of the correctness of their arguments.

At all stages the coalition of patient groups campaigning for the amendments that would permit research were careful to keep

their membership informed – to the extent that a number of individuals went to see their MPs to explain in detail why they supported this research and what their hopes for it were.

Throughout the process there was a transparent partnership between the collaborating charities and also with officials in government departments so they would know what to expect and be alive to the patient’s viewpoint. This careful, measured approach has been a valuable confidence builder in developing a long term relationship between patient groups, legislators and officials which will be important in the future as this line of research develops and moves into the treatment phase.

In itself this will provide support for stem cell research in the UK, whilst helping to ensure leverage for research findings both within the UK and internationally to sustain progress in the field.

A constructive, respectful and principled approach by patient groups in the UK, was an important factor in giving legislators the confidence to move in the direction being recommended by experts, despite the fact that the issue was widely held to be sensitive and one which if handled badly could rebound to the disadvantage of all concerned.

Hopefully the fact that a rational, logical and courteous debate on such an issue was possible will provide a lasting benefit for the UK parliamentary process and for other legislatures elsewhere.

## 6 – Discussion and Conclusions

Discussion of the issue was wide ranging and unconstrained. A number of general principles emerged at the start that most, if not all participants appeared to accept as common ground from which to build. These are :-

- Research using embryonic stem cells is a very important area of current bio-medical investigation. It holds out significant prospects for creating new therapies for a number of serious and life threatening conditions for which there is currently no cure or effective treatment.
- Respect for the embryo is required but it is not absolute. The departure from that which would be afforded to a fetus or a baby is justified by reference to the desirability of the goal which research is pursuing and the potential benefits for human health that may result.
- Research using embryonic stem cells needs to proceed in parallel with that on adult stem cells. The lines are complementary and it is not clear that adult stem cells will replace or make redundant the use of embryonically derived stem cells.
- Once established, embryonic stem cell lines are no longer embryos. They have a different moral status and it is not appropriate to regulate research and development on them as if they were still embryos.
- Any difference between “spare” embryos and embryos created for research purposes may be more those of perception and public reaction than grounded on observed and objective “facts”. Nevertheless, so long as there is an adequate supply of spare embryos to meet all legitimate research needs, the justification to proceed with the creation

of embryos using cell nuclear replacement techniques may be somewhat reduced. However, should the situation change or should there be particular therapeutic advantages to be gained through CNR techniques then this would no longer hold. The defining characteristics for the framework for decisions regarding spare or created embryos should be safety and clinical need.

Given the fact that the use of embryonic stem cells in research causes anxiety (and outright condemnation) in some vocal sections of the community, it is appropriate that public confidence and support is maintained and an appropriate regulatory framework is developed. The UK Gene Therapy Advisory Committee offers one possible model, giving approval to research proposals on the basis of the seriousness of the disease at which the research is targeted, the quality of the science proposed and the ethical acceptability of the approach to be adopted. Whilst it is clear that this body could not simply be extended or transplanted into other jurisdictions, nevertheless experience of its operation has given valuable experience which could be built upon.

Another area where there is likely to be considerable manifestations of unease is over the issue of patents and intellectual property. This is an area where there is much scope for misunderstanding and misrepresentation of the issues. In Western economies it is clear that some form of patent law is an essential tool in the development of research findings into useable products it is the case that the notion of an embryonic cell line itself being patentable is one that is one that will cause for concern in some quarters. Biotechnology patents will be a continuing flash point for discord unless a determined effort is made to give the public the real information they need to form a view on this issue. Then if there is widespread concern there may be cause to act and re-visit existing legislation in this field.

Ethical, moral and religious differences within and between member states will make harmonisation impossible in any meaningful way for the foreseeable future. At least until clear therapeutic solutions have emerged this will continue to be the case. So long as the work is in the research phase a country by country approach seems to be the best way forward – recognising that, if solutions to serious health problems do emerge, pressure is likely to be in the direction of making them available, not vice-versa. Meanwhile a consistent communication strategy should be put in place to keep the public informed.

It is suggested that the elements of such a strategy might emphasise the following themes (amongst others):

- The high natural wastage of early embryos
- The image of the blastocyst (to bring home the point that these are not tiny babies)
- The interweaving of ethical and safety issues (to stress that things that are not safe are not ethical but research may make them safe and therefore ethical but things that are not ethical remain unethical even if they are safe).
- That the knowledge and the technology exist and cannot be uninvented.

Commissioned surveys of public understanding and attitudes will highlight what is known and what is thought. This will facilitate the construction of information and educational programs that address real concerns (whether based on biological plausibility or not)

Scientists need to see public communication as part of their work. This requires a commitment to dialogue and whilst the research gives grounds for optimism about future benefits, care must be taken not to over-hype this potential if the public are not to lose trust in the information they have been given. At the same time, dealing with the communication of risk and uncertainty is difficult, especially in a culture which seems to be risk averse – at least with respect to contemporary science.

A legal framework for decision making within which costs and benefits, risks and opportunities can be logically evaluated needs to be established – probably on a state by state basis. Ideally this should be at arms length from the political process to avoid short-term opportunism and grandstanding and capable of dealing quickly and fairly with issues such as

- Research bottlenecks
- Developing regulation in the light of new biological possibilities
- The involvement of stakeholders
- The role of pressure groups (for and against)
- The education of the public
- Macro and micro level pluralism

Clearly informed consent for embryo research is essential. The extent to which research using embryonic stem cell lines requires further consent once approved by the donor to establish them has been unclear. It is not obvious that these require separate procedures from other types of research using human tissues and whether embryonic stem cell lines have any superior moral status by virtue of their origin over other human tissues that have been immortalised. The issue of consent has a bearing on the question of ownership. Clearly consent does not necessarily imply ownership but it relates to the allocation of intellectual property rights and the desirability of creating a mechanism for recognising social as well as financial returns arising from the development of products based on stem cell technologies.

There seems to be a difference between the public's regard for spare embryos and those created for research purposes. However, it is arguable that there is an important conceptual and emotional difference between the two that reflects the purpose for which the embryos were originated. (*ie* created embryos were instrumentalised from the start and therefore do not carry the same level of emotional engagement as those which were produced possibly for the purpose of becoming a baby).

Consideration of this question in turn leads to further thought as to the moral status of the embryo and of any stem cell lines derived therefrom. However we define the moral status we must recognise that most religious and ethical codes allow for the taking of life under certain circumstances – soldiers in war, abortion when the mother's life is at risk – the sacrifice involved

must be necessary and proportionate to the circumstances. Embryonic research requires a compromise between respect due to a potential life to be contrasted to the respect owed to someone who is alive and stands to lose their life by virtue of our decision not to act – not to permit research to proceed.

For stem cell lines, as opposed to embryos, their moral status seems to derive from what is invested in them by virtue of the fact that they arose as a result of a sacrifice. Clearly the embryo itself is incapable of suffering. Its existence is below the line at which suffering is capable of occurring. Nor does it have any capability to allow it to contemplate the issue and form a view. The notion of legal “suffering” (*ie* harm to its interest without being aware of it) does not seem to be particularly helpful here as a route to resolving this question. Ultimately the decision whether or not to proceed with embryonic stem cell research is a political one. Ethical arguments do not lend themselves to an instrumental political debate. Such debate will take place against a scientific consensus that the research is promising significant progress by routes not available elsewhere and in the light of an impossibility of meaningful harmonisation at European level. This said it does seem possible to draw up a series of parameters that would appropriately define “respect” due *ie*

- Europe demonstrates moral plurality on this issue.
- Existing legislation already creates mechanisms for respecting embryos that acknowledge this diversity.
- Embryonic stem cell lines are different from embryos by virtue of the fact that the possibility of constructing a baby from them has been removed. Their moral status is therefore held as a proxy.
- It is not clear the extent to which embryonic stem cell lines differ from other human cell lines (if at all). Nor is it clear that the public has clearly formed and differentiated views on this topic.

Whilst the availability of spare embryos for research (there are over 100,000 stored in freezers in the EU) can hide the need to create embryos, it must not be overlooked that the existence of spare embryos is not inevitable and some states (*eg* Germany) prohibit the creation of embryos that will not be implanted. Furthermore as IVF technology improves, the number of spare embryos will fall. Also some types of treatment will require the creation of embryos by CNR so it should not be ruled out on grounds that may subsequently need to be reviewed. The guidelines should be to use as few as possible as efficiently as possible in ways compatible with good science. This is more important than differentiating by source.

Immortalisation of donated embryos by virtue of their use in the creation of cell lines may raise issues for some donors. Hitherto donors knew that embryos would be destroyed and that as a result there would be the possibility of “closure”. Furthermore their embryos would be used in research that was close to their own experience, often carried out by embryologists who had helped them directly. Whether these factors will be significant when the creation of stem cell lines is proposed is unclear.

When research is promising there can be a temptation to extrapolate too far and to move from *in vitro* to *in vivo* work in humans too quickly. Animal models should be used where

relevant and appropriate to test out hypotheses. However there are a number of known inter-species differences that cannot be addressed using animal models and some things will have to be tested out for the first time using human volunteers. From the perspective of the patient it can be argued that the wrong question is being addressed by emphasising caution. Rather we should be trying to move things forward faster, accepting the possibility of risks in the search for effective cures before more people die prematurely – remembering that all the normal approvals prior to undertaking research in human subjects still apply, including peer review of quality and relevance, ethical committee approval as well as any other current regulations in force.

The importance of public endorsement for this research is apparent to anyone who witnessed the reaction to the GM foods issue. To engender this trust is not a one-off exercise. Rather it is an ongoing process that will involve regular explanation of what is going on and how it is important. The role of the media is important and they need to be engaged in presenting the story if chances of misperception are to be reduced. It is virtually impossible to correct a false impression once it has been balanced.

Because science and scientists are generally losing public trust and confidence funding should be identified for programs of public engagement in the understanding of the nature of science and the risks and benefits associated with it across the EU. Patient groups have an important part to play in this and they too need to be resourced to enable them to fulfil this role.

However this is not a one way process. Scientists must acknowledge the reality of public concerns, even if they believe them to be implausible or based on misunderstanding. Failure to do this will distance scientists from their society and promote suspicion, rather than generating support for medical research. In this way it ought to be possible to spot the elephant traps in the road ahead and avoid them, fill them in or bridge them over for the benefit of patients and their families needing science based solutions to life threatening health problems.

Given the importance of this research and the potential it holds out the European Institutions should recommend to the member states that consideration be given to putting in place an appropriate national regulatory framework. However care should be taken to avoid premature or too heavy handed restrictions that will close down opportunities prematurely. The mere fact of regulating may also be taken as evidence of the reality of some people’s concerns. After all, the reasoning goes, if it wasn’t necessary, they wouldn’t do it would they?

Finally, the principle of subsidiarity should not be lightly abandoned. The impossibility of harmonisation should be clear, but this European diversity should be embraced. If member states have gone through their own due process then the validity of the conclusions reached be respected and endorsed as right for them. This will bring mutual benefits and is part of the added value that comes from being part of the European Community. This, ultimately will be the soundest route for determining whether the promise that this research is holding out is real and whether it can be realised for the benefit of all who need and wish to in the European Community.

**Annex I – Programme***Friday 14th September*

- 18.00 Arrival and registration  
20.00 Dinner and Introduction to the workshop.

*Saturday 15th September*

- 09.00 Welcome from the chair and brief introduction of delegates  
09.15 An introduction to the science.  
10.00 An ethical framework  
10.45 Coffee  
11.15 Workshop 1  
12.30 Lunch  
13.30 Regulatory and Legal Issues  
14.15 Workshop 2  
15.45 Tea  
16.00 The patients' view  
16.45 Workshop 3  
18.00 Break  
20.00 Dinner and Guest Speaker

*Sunday 16th September*

- 09.00 Feedback from workshops by rapporteurs  
10.00 Discussion of areas of agreement/difference and determination of actions  
11.00 Preparation of "Summary Statement"  
12.00 Close of meeting  
12.30 Buffet Lunch and depart

**Annex II – List of participants**

- Dr Segolene Aymé.....INSERM, France  
Dr David Bennett.....European Federation of Biotechnology Task Group on Public Perceptions of Biotechnology  
Professor Richard Braun.....University of Bern  
Rev Dr Kenneth Boyd .....University of Edinburgh  
Prof Jean Jacques Cassiman ..University of Leuven Belgium  
Ms Veronica English .....British Medical Association  
Ms Laura Gilbert.....Public Affairs Manager, Bio Industry Association  
Mr John Gillott .....Policy Officer, Genetic Interest Group  
Ms Andrea Gondová.....European Federation of Biotechnology Task Group on Public Perceptions of Biotechnology  
Dr Harry Griffin.....Roslin Institute  
Ms Rachel Haynes .....Parkinson's Disease Society  
Mr Alastair Kent .....Genetic Interest Group  
Dr Adam Hedgecoe .....University College London  
Prof Ulf Kristoffersson .....University of Lund, Sweden  
Dr Graeme Laurie.....University of Edinburgh,  
Ms Catherine Levinson.....Serono International SA  
Mr Robert Meadowcroft.....Parkinsons Disease Society  
Ms Elly Muilman .....Technical University of Delft, Netherlands  
Dr Christine Mummery.....University of Utrecht  
Drs Patricia Osseweijer.....Technical University of Delft, Netherlands  
Mr Andrea Rappagliosi.....Ares-Serono International S.A  
Dr Darren Schickle .....The University of Sheffield, School of Health and Related Research  
Ms Juliet Tizzard .....Progress Educational Trust  
Dr Timo Tuuri.....Family Federation of Finland  
Mr Hugh Whittall .....Human Fertilisation and Embryology Authority