

The Rationale for a Registry of Clinical Trials Involving Human Stem Cell Therapies

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Human embryonic stem cells (hESC) are pluripotent cells that are capable of self-renewal and can differentiate into nearly any type of cell in the body.¹ At present, it seems that early embryos are the best source of suitable stem cells as they are “the only pluripotent stem cells that can be readily isolated and grown in culture in sufficient numbers to be useful.”² Few scientific discoveries have elicited more enduring concerns among scholars, government officials and the general public than the permissibility of conducting research on embryos in general, and on hESC in particular. Governments are confronted with the vexing question of how to balance the beneficial therapeutic prospects of hESC with complex socio-ethical and moral issues.

Much of the ethical and policy debate surrounding hESC research focuses on the moral status of the human embryo: should the human embryo be recognized as a potential person or, at minimum, be given particular legal protection? It is clear that there is no simple answer. In fact, it has proven to be difficult to render an account of when human life begins and what moral – and, *a fortiori*, legal – status should be ascribed to the human embryo.³

Amidst all the controversy, researchers are in the process of studying how embryonic stem cells can be used to alleviate human suffering through the development of tissue and organ therapies (regenerative medicine). Embryonic stem cell research promises new therapeutic applications as well as medical and cosmetic (non-therapeutic) applications, such as genetic enhancement. At the present time only haematopoietic stem cells obtained from bone marrow

and blood cell precursors are used in stem cell therapy. Embryonic stem cell research, on the other hand, is only in the initial stages of development and is not yet at the clinical trial stage. Moreover, there are insufficient clinical grade stem cell lines available for stem cell research to progress to the clinical stage without putting the safety of human subjects at risk. Researchers are still trying to perfect how to derive and control embryonic stem cells, but it will not be long before these human tissues are widely used in clinical trials.⁴

Therefore, with the promise of new therapeutic interventions involving stem cell lines and the increasing permissibility of stem cell line procurement worldwide (from supernumerary IVF and/or cloned embryos),⁵ it is important that ethical and safety issues are not overlooked when developing public policy concerning stem cell research. All eventual stem cell clinical trials must be transparent and follow high quality standards in order to ensure the safety of human participants. In order to promote transparency and accountability, registries have been created internationally to disclose minimum data from human clinical trials, regardless of whether the outcomes are positive or negative. With the additional safety concerns that surround stem cell clinical trials, it would then be important to explore the feasibility of creating a clinical trial registry specifically for stem cell clinical research.

This paper will provide (1) an overview of the rationale behind clinical trial registries; (2) a summary of the ethical and scientific objectives of clinical trial registries; (3) a



discussion on whether stem cell clinical trial registries have special issues to consider; (4) a survey of the challenges concerning the implementation of stem cell clinical trial registries; and finally (5) suggestions for possible stem cell clinical trial registry platforms.

1. The Rationale for Clinical Trial Registries and the Development of International Standards

The growing concern regarding publication or selection bias – a common practice in the scientific community by investigators, peer reviewers, journal editors, funding bodies and research sponsors – has sparked the need for clinical trial registration. Study results that demonstrate risks or clinically important negative trial outcomes are left underreported⁶ while there is an overemphasis on benefits.⁷ Trial results “that are statistically significant, interesting, from well-funded studies, or of higher quality are more likely to be submitted, published, or published more rapidly than work without such characteristics.”⁸ As a result, new interventions, that may be more expensive, are often promoted and adopted at the expense of treatments that may be safer or more effective.

In the past, harmful consequences have resulted from unreported or unpublished trial outcomes. For example, in the 1980s, systematic reviews of antiarrhythmic drugs performed by Furberg and colleagues revealed that the drugs caused sudden death for patients with ventricular arrhythmias. The results of these studies were not substantive enough to convince scientists and physicians to abandon the use of the drugs so the negative results went unreported. Making the dangers of the antiarrhythmic drugs known would have prevented the reported 20000 to 75000 deaths per year between 1983 and 1993, when the report was finally published.⁹ More recently, a systematic review published in 2004 demonstrated that a major pharmaceutical company had repeatedly committed fraud when it did not report the true efficacy of an antidepressant drug.¹⁰ The potential harms of publication or selection bias illustrate the importance of transparency in clinical trials.

Clinical trials have great potential for improving medical practice but this can be achieved only if they are evidence-based. If the conduct and outcome of clinical trials are not comprehensive and transparent, public trust in science will erode. Past scandals related to publication or selection bias have led to international standards and the adoption of policies by international organizations,¹¹ journal editors,¹² medical associations,¹³ and even industry¹⁴ to recognize the importance of clinical trial registries. International and na-

Figure 1: Examples of Current Policies for Clinical Trials Registries

1. The International Committee of Medical Journal Editors (ICMJE) (2004)

ICMJE mandates that, as a condition of publication, all clinical trials (except Phase I) beginning enrollment after July 1, 2005 be registered. ICMJE requires that registries are owned and operated by not-for-profit organizations, contain a minimal data set consisting of 20 items and be accessible free of charge by the public.¹⁵

2. World Health Organization (WHO), *International Clinical Trials Registry Platform (ICTRP)* (2006)¹⁶

Developed in collaboration with the International Standard Randomised Controlled Trial Number (ISRCTN) register, based in the UK, and the ClinicalTrials.gov registry, based in the US, the ICTRP aims to promote consensus regarding international norms and standards in clinical trial registration, which includes a minimum registration dataset. The ICTRP requires that clinical trials are registered at inception and proposes that a unique *Universal Trial Reference Number* be given to each trial to prevent duplication. The ICTRP is not a registry itself but a comprehensive search portal for registries that exist worldwide.



Figure 1: Examples of Current Policies for Clinical Trials Registries — *continued*

3. **Ottawa Group, *Ottawa Statement* (2005)**¹⁷

The Ottawa Statement is a consensus document that outlines key principles regarding human clinical trial registration. The recommendation includes a minimal registration dataset which goes much further than the requirements of the WHO. This statement requires the trial protocols be disclosed from the beginning, disclosure of all amendments along the way, and the posting of final results. This statement has the support of 100 individuals and organizations worldwide¹⁸ but does not yet have support from the pharmaceutical community.

4. **The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), along with the European Federation of Pharmaceutical Industries and Associations (EFPIA), the Japanese Pharmaceutical Manufacturers Association (JPMA) and the Pharmaceutical Research and Manufacturers of America (PhRMA), *Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases* (January 2005) and the *Joint Position on the Disclosure of Sensitive Information via Clinical Trial Registries* (2005)**

The pharmaceutical industry commits to registering information about all new and ongoing industry-sponsored clinical trials, other than “exploratory trials” (*i.e.* trials that generate or test hypotheses), in a free, publicly accessible clinical trial registry. The WHO “minimum data set” will be adhered to but the following data may be considered “sensitive” by the sponsor who may wish to delay the release of information for “competitive reasons”: primary outcome, key secondary outcomes, intervention, target sample size, and official scientific title of the study.

5. ***The Latin American Ongoing Clinical Trial Register (LATINREC)***¹⁹ (2003)

This registry is being developed by the Colombian Branch of the Iberoamerican Cochrane Network in order to “collect information on clinical trials undertaken in Latin American countries, make this information available to the public, and provide methodological informational and other tools as required by trialists.” The registry is available online at: www.Latinrec.org. All clinical trials must be registered according to the ICTRP data set and must receive a unique identification number assigned by the WHO.

6. ***Ethics Review Boards*** (ERBs) – some require registration of clinical trials as a condition of ethics approval.²⁰

7. ***Regional or national laws*** requiring trial registration (*e.g.*, European Union,²¹ USA,²² UK²³ and South Africa).²⁴

tional policies have made clinical trial registration a priority. Examples of policies are found in Figure 1.

2. Ethical and Scientific Objectives of Clinical Trial Registration

A Clinical Trial Registry (CTR) is widely defined as a database of all human interventional clinical trials²⁵ regard-

less of the stage of development – at inception (when funding has been secured or prior to participant recruitment), while in progress or after completion – whether it has been published or not. Main features of the CTR database encompass the trial’s objectives, main design features, sample size, and tested treatments.

Aside from avoiding the negative consequences arising from publication or selection bias, CTRs achieve many important scientific and ethical objectives (Figure 2). An emerg-



ing consensus finds that the prospective registration of all interventional trials is a scientific, ethical and professional responsibility – if not a legal obligation – for scientists, governments and funding organizations.²⁶ Some authors consider the failure to fully report clinical trials “scientific or professional misconduct” and state that researchers have a moral obligation to report all trials involving human subjects.²⁷ It has also been suggested that “prospective trial registration should be a legally required component of written informed consent.”²⁸ This duty is grounded in the fundamental need to disseminate knowledge and protect, as well as respect, research participants and patients.

Figure 2: Objectives for a Clinical Trial Registry²⁹

1. *Disseminate information/knowledge transfer*
2. *Respect the investigator-participant covenant to contribute to biomedical knowledge by making trial methods and results public*
3. *Provide a foundation for evidence-based medicine*
4. *Enhance accountability and transparency with regard to standards in ethical research*
5. *Promote improved allocation of resources*
6. *Protect/respect research participants*
7. *Prevent wasted and unnecessary duplication of research*
8. *Enable monitoring of adherence to ethical principles and process*

CTRs will facilitate access to the results of clinical trials in a comprehensive and objective manner³⁰ and further accelerate dissemination by making information publicly available. Furthermore, it is suggested that CTRs will provide the public access to new studies and a platform to conduct meta-analyses,³¹ which will encourage communication and collaboration between researchers, accelerate the research process, prevent duplication of research and promote patient recruitment in trials.

Ultimately, the *raison d'être* for the establishment of a CTR is found in the notion of benefit sharing. The prospective registration of clinical trials would fulfill the expectations of both funding agencies and research participants since it will contribute to society's collective knowledge. Research involving human participants cannot be justified as contributing to the social good unless the resulting knowledge from the studies is shared.³²

As numerous individual clinical trials have inadequate statistical power to adjudicate reliably between alternative treatment strategies, meta-analyses or quantitative overviews of all relevant trials are necessary to draw conclusions about the efficacy of a particular treatment or procedure.³³ Such trials are the primary means by which the safety and efficacy of new drugs and other interventions are assessed. Their results have improved clinical practice in many areas of medicine.³⁴ However, since many of these meta-analyses are based on a summary of only the published trials, they are susceptible to the problem of publication bias.³⁵ By requiring the prospective registration of clinical trials at their inception, the problem of bias in the body of evidence could be largely eliminated, as registration in a CTR would occur independent of the ultimate findings or publication status of a trial.

Professional organizations rely on the body of scientific evidence to draft best practice guidelines, which in turn outline the current standard of care. Likewise, policy-makers often rely on such evidence when drafting laws and regulations dealing with scientific and medical practice. Consequently, a CTR could have a great impact in shaping not only public policy, but also medical or product liability.

Of equal importance is the objective of increasing the protection of patients and research participants. Another crucial objective of a CTR is to build, restore and maintain public trust in the integrity of scientific research by ensuring accountability and transparency of clinical trials results. Today, public trust is the cornerstone of sustainable scientific research. Furthermore, transparency and accountability in the conduct and the dissemination of clinical trials at any stage, by means of registration in a CTR, fosters public respect for those who have participated and by those who rely on biomedical research.

The principle of autonomy underlies the doctrine of informed consent. For research participants to be respected as autonomous agents, they must provide free, voluntary and informed consent. Most often, the participation of healthy



volunteers in a clinical trial takes place because such individuals believe they are contributing to the generation of medical knowledge (which could eventually translate into cures and therapies). However, when the knowledge gained is never transferred, the trust between research investigators, research participants and the public at large is breached. Ethical concerns are heightened when the breach of trust (and autonomy) takes place in the context of trials that provide financial gains for the industry.

Finally, an additional advantage of a CTR is that it will foster better allocation of resources, informing priority setting and the future of research by identifying trends and gaps. By providing information regarding planned, ongoing and completed clinical trials a CTR will facilitate the planning of new studies and the use of resources by avoiding the duplication (which must be distinguished from appropriate replication) of research.

While scientists have had long-standing concerns about the phenomenon of publication bias, the rise of evidence-based health care and its dependence on systematic reviews and meta-analyses has made this problem more pressing. A CTR would have the important objective of contributing to the foundation of evidence-based medicine and the improvement of clinical practice by supporting the translation of research from the bench to the bedside through the development of best practice guidelines.

3. Clinical Trial Registry for Stem Cell Research: A Special Issue?

There are, therefore, compelling reasons for supporting the establishment of a CTR. What remains contentious however is the existence of an equally compelling rationale that warrants a special clinical trial registry for stem cell research. This issue has seldom been addressed despite the fact that clinical trials are currently in progress using adult or foetal stem cell lines.³⁶

The translation of stem cell therapy from laboratory to clinical applications poses unique challenges. These challenges range from ethical and policy implications to scientific concerns for safety, quality and efficacy. Ethical debates surrounding stem cell research relate to controversies about the use of embryonic stem cells in research; some argue that the embryo has special moral status and should be protected. Therefore, the creation of a unique clinical trial registry for stem cell research could address these ethical issues pro-

vided that the registry includes information regarding the origins of the stem cell lines. A registry for clinical trials regarding stem cell based therapies should disclose the provenance of stem cell lines – whether embryonic or not – in order to respect prospective research subjects or patients' beliefs regarding the human embryo's moral status. Only with information regarding its source can the public make informed decisions regarding whether or not to participate in a trial, or receive future therapy or treatment.

Requiring that the provenance of stem cell lines be disclosed in a stem cell clinical trial registry could also decrease risks to research participants. For instance, insufficient certainty about the origins or traceability of the stem cell lines can have detrimental effects on the safety and health of the participants or patients involved.³⁷ Safety concerns relating to stem cell use include the risk of infectious diseases, the transfer of genetic disorders and the manner in which the stem cells are manufactured and stored.³⁸ For example, the concern regarding additional risks for infectious diseases results from the fact that many human stem cell lines created to date have been contaminated with animal cells because they were cultured using mouse feeder layers.³⁹ Therefore, the central question becomes whether it would be prudent to await the development of new clinically grade stem cell lines before embarking on human stem cell trials. This would then ensure maximum protection for the first human research participants.

As stem cell research continues to evolve, it is important to implement policies requiring that stem cell sources are reliable and that manufacturing and storage practices respect standard quality control measures. Existing stem cell banks, such as the UK Stem Cell Bank, aim to provide researchers access to ethically sourced stem cell lines that have been cultured, preserved and characterized under strict guidelines to guarantee their authenticity and quality. With these stem cell banks, researchers have access to high-quality stem cell lines for use in clinical trials. However, if these clinical trials are not registered, the necessary follow-up and traceability of the stem cell lines and their use could be limited. Similarly, the disclosure of the trials' outcome could be limited or null. Like all other clinical trials registries, the registration of stem cell clinical trials will foster transparency and accountability. Existing stem cell banks can serve as an instrument through which these trials can be registered. In this way, the entire supply chain of stem cells from donor to the recipient in the clinical trials can be documented and traceable. This point will be developed further in the following sections.



Figure 4: A Clinical Trial Registry for Stem Cell Research: A Special Issue?

1. Cell line derivation, characterization, delivery and banking
2. Safety, efficacy and quality standards
3. Translational research
4. Traceability/Origins of cell lines
5. Compliance of diverse/conflicting international policies
6. Policy regarding the registration of clinical trials at different phases

Figure 5: The Rationale for a Clinical Trial Registry Involving Stem Cell-based Research

1. Maintain respect for research participants
2. Foster accountability with regard to global standards for ethical research
3. Encourage adherence to ethical principles and processes
4. Provide global open access to information
5. Provide unbiased public records on safety and effectiveness
6. Foster innovation and acceleration of research practice in clinical therapies
7. Increase opportunities for collaboration and participation
8. Maintain public trust

4. Challenges for the Implementation of a Stem Cell Clinical Trial Registry

Many questions must be addressed and analyzed before implementing and managing stem cell clinical trial registries. In order to be effective, a stem cell clinical trial registry must be global, comprehensive, accurate and publicly accessible. In addition, access to a registry should be simple, inexpensive and appropriate to the intended user population to allow for the unrestricted dissemination of research results. All these requirements should be coupled with an independent verification of postings and compliance mechanisms in order to ensure that ethical standards in clinical practice are respected.

a. Objections to Clinical Trial Registration

The design, scope and the implementation of a registry must be guided by the needs of the primary intended users, patients and other members of the public. The success of a registry would also ultimately depend on a willingness to contribute to a joint enterprise for the common good.⁴⁰ Because the pharmaceutical and biomedical industries are responsible for funding the majority of clinical trials, it is essential that these industries participate in and comply with registration standards. They may be reluctant to register clinical trials because of the adverse effects on intellectual property rights, commercial or academic competitive advantage, the danger of international piracy and/or the disclosure of trade secrets. These objections could result in targeting the therapeutic development and regulatory strategies of companies, damaging investor interests and stock value.⁴¹

It is argued that, due to the confidential nature of certain registration data, delayed disclosure of trial data should be permitted. However some authors contend that there is a lack of evidence supporting arguments for delayed disclosure.⁴² Clinical trials are public by nature and any information that is claimed to be sensitive is readily accessible through trial participants and consumer websites. Furthermore, it is also argued that transparency and openness in the scientific field does not hinder innovation but instead promotes it. "Knowing how to capture innovation's benefits requires rethinking old assumptions about creation and ownership."⁴³

The pharmaceutical and biotechnological industries concede that the dissemination of knowledge and the protection of the safety of patients (and research participants)



must triumph over concerns for the confidentiality of proprietary interests, the protection of academic freedom and the exclusivity of research ideas.⁴⁴ However, they argue that a clinical trial registry would not have the effect of increasing safety or protections for research participants/patients, nor of diminishing publication bias.

It remains to be seen if a balance between those conflicting interests could be achieved in order to serve the public interest. As pointed out by Rennie, “the financial cost of an effective, independent and transparent clinical trial register would amount to a tiny fraction of the costs of the trials themselves, or the costs of not knowing their results, while the personal costs of allowing the present chaotic system to continue are incalculable.”⁴⁵

b. Implementation of Compliance Mechanisms and Oversight

In order to encourage compliance by biotechnology and pharmaceutical companies, a middle ground can be agreed upon which would allow companies to withhold key information concerning the clinical trial but still require that trials be registered at all phases. A relevant question to explore is what should be considered key information and who should have the authority to define what information should be disclosed.

At the present time, registration of clinical trials is generally voluntary, making compliance mechanisms difficult to enforce. However, there are policies adopted by different countries or institutions aimed at making registration a requirement. At the local level, there are some countries that have adopted laws that make the registration of all clinical trials mandatory.⁴⁶ Institutions at the international level have also made registration of clinical trials a requirement. Unlike the WHO’s Clinical Trial Platform, which is based on voluntary registration, the International Committee of Medical Journal Editors (ICMJE) mandates that any paper on clinical trial results must be recorded in a publicly accessible registry before it can be published.⁴⁷ The ICMJE, an organization which represents eleven renowned medical journals, has thus taken the initiative to prevent publication bias while giving researchers an incentive to register their trials.

Aside from implementing compliance mechanisms, the auditing, monitoring and oversight of the registries are additional difficulties that must be overcome in order for the registries to be effective. Similarly, safeguards to maintain

privacy and confidentiality of research participants and proprietary information must be established. A registry includes extensive data coming from multiple sources; it requires frequent updating to remain thorough and correct. Therefore, verification procedures must be enforced to ensure accuracy and quality assurance. With regard to the implementation of stem cell trial registration, it would be essential that an independent party validate registrants, assess risks, and establish quality and safety standards. All cell lines intended for human clinical trials should be traceable and their origins should be proven and inspected by accredited agencies to establish the risk involved at all stages of development and production.

It is recommended that the responsible authority with the mandate to monitor and oversee the registry should be given to an independent non-profit third party, such as an institutional or ethics review board that already has the role of approving research protocols. The Steering Committee for the UK Stem Cell Bank, the International Society for Stem Cell Research (ISSCR) or the International Stem Cell Forum (ISCF), three independent organizations that already oversee or will be overseeing stem cell banks, could also be given the mandate to administer stem cell registries given that stem cell lines used in clinical trials will most likely be procured from these stem cell banks. Having an independent third party monitor the register for completeness and compliance will prevent conflict of interest issues since there will be no outside influence from funding organizations.

c. Time of Registration and Implementation of a Minimum Data Set for Stem Cell Clinical Trials

Important issues to consider regarding the implementation of a stem cell clinical trial registry would include: what information should be disclosed, at which phase the clinical trial should be registered and whether delaying disclosure should be allowed. One of the objectives of clinical trial registration is to promote transparency and this could be accomplished by providing raw and anonymized datasets for public scrutiny. Many researchers are concerned that making raw data public may lead to inappropriate analyses and misinterpretations.⁴⁸ However, it is argued that this would be the “ultimate form of peer review” as it would ensure that “every statistician will have to prepare reports knowing that they will be scrutinised in the finest detail by a frequently hostile posterity.”⁴⁹



It is also argued that clinical trials should be registered at all phases, even at inception, in order to ensure safety and efficacy. Without the registration of clinical trials at all phases it would be impossible to know the adverse reactions or true effectiveness of a drug because unfavourable findings could easily be suppressed. The registration of early-phase clinical trials would then ensure that the risks related to new interventions or treatments would be publicly known.⁵⁰ If clinical trials are registered only after they have been completed, found to be favourable or published, publication bias will result. Furthermore, requiring that clinical trials be registered at inception would prevent the loss of potentially valuable scientific information, as early trials are often terminated for economic reasons.⁵¹

Particular challenges relate to the design and scope of a clinical trial registry for stem cell lines, especially concerning the establishment of a minimum data set as it would require agreement on standard data elements. A mandatory, minimum data set fosters transparency and accountability by providing a comprehensive and transparent (non-promotional) posting of methodology and results. The currency and accuracy of the information in a prospective registry is of paramount importance. In the case of stem cell clinical trials, including data regarding the origin, for traceability purposes and storage procedures of the stem cell lines, it is necessary to ensure that patient safety is not compromised.

The registration data set proposed by the WHO's ICTRP could be used as a model, but additional information regarding the stem cell lines in particular should be included. Stemming from the information required by the WHO, the ICMJE, and organizations that maintain registries specific to stem cell lines, such as the UK Stem Cell Bank, a comprehensive minimum registration dataset for stem cell clinical trials would include the following key information (Figure 7).

4. Possible Platforms for Stem Cell Clinical Trials Registries?

Overall, the coordination and monitoring of a de novo centralized stem cell registry would be very difficult because of the need for considerable resources and the substantial costs involved. The difficulties of managing a massive scope of data coming from multiple sources, accompanied by the need for regular updates to guarantee accuracy and completeness, present great financial and technical challenges

Figure 7: Disclosure Requirements (model)

Standard Clinical Trials:

1. Trial name or title
2. Unique Registration number
3. Registration Date
4. Disease or condition concerned
5. Objectives
6. Outcomes (main and secondary)
7. Intervention(s), treatment(s)
8. Secondary IDs
9. Sponsor and funding sources
10. Responsible contact person
11. Research contact person
12. IRB review

Stem Cell Clinical Trials:

1. Type (embryonic, foetal, adult)
2. Classification (research grade/clinical grade stem cell lines)
3. Unique bank accession number
4. Donor selection criteria
5. Microbiological screening of the donors
6. Records of tissue/cell removal and desegregation
7. Cell harvesting and preparation
8. DNA fingerprinting or profiling (confirm origin of cell line and check for cross contamination between cells)
9. Type, source and batch numbers of media additives
10. Origin, history and other details of any feeder layers used
11. Methods used to establish cell line (including the population doubling times, split ratios and passage number)
12. Microbiological status (including the nature, use and removal of antibiotics)
13. Characteristics (e.g. surface antigen expression, gene expression, DNA fingerprinting, RNA analysis, etc.)
14. Quality systems employed to assure safety and quality
15. Informed consent obtained from donors
16. Licences, approvals, and accreditations
17. Research Ethics Committee approval/Supervising authority



that need to be addressed at the outset. Furthermore, there already exist vested interests in independent or local registries that have their own objectives or goals, which present logistical challenges in building a centralized registry. Creating a new and separate registry would also cause unnecessary duplication of data and information.

A possible solution would be to build a network linking existing stem cell banks or those that will be created in the future. The International Clinical Trials Registry Platform, already established by the WHO, could be a convenient starting point to disseminate information on stem cell registries or stem cell banks since it would be manageable to include a sub-category specific to stem cell clinical trials. Using the WHO's platform would also ensure quality control because, in order to be included in the database, registries must follow certain standards and requirements recommended by the WHO. For example, the WHO has developed draft criteria to become a "primary register," which include: collecting all items listed in the registration data set, performing quality assurance on submitted entries, establishing a process for obtaining updated data and ensuring that there exist deduplication procedures for the various registries.

Another option is to use existing stem cell banks as a point of initiation to collect information on stem cell clinical trials. Due to the lack of clinical-grade human embryonic stem cell lines, stem cell banks were created to ensure the quality, traceability and safety of stem cell lines.⁵² There are international initiatives developing standards for the derivation, characterization and maintenance of human stem cell lines. Most notable is the effort by the International Stem Cell Forum (ISCF)⁵³ and the International Society for Stem Cell Research (ISSCR). However, other stem cell banks already exist or are in development. Examples of existing or proposed stem cell banks that could serve as platforms are given below (Figure 8).

These stem cell banks already provide data on the origins of each stem cell line and, as researchers begin to embark on stem cell clinical trials, it would be practical to use these same banks to trace how each particular stem cell line is used in a specific clinical trial. If organized as a harmonized consortium, these stem cell banks can serve as a single search portal for any researcher or member of the public to obtain information on where the stem cell line originated, how it was stored and whether it is being studied in a clinical trial. Provided that the ISCF and the ISSCR develop registries coordinating international stem cell banks, their stem cell banks would be the ideal place to begin register-

ing stem cell clinical trials. Another option would be for the UK's Stem Cell Bank to take the lead in such an effort since it has a well-established governance structure and has obtained international recognition.

Conclusion

With stem cell research still in the early clinical stages and insufficient clinical-grade stem cells available for clinical use, some may argue that the establishment of stem cell clinical registries is premature. However, the scientific community is rushing to discover different sources of stem cells and to perfect the derivation and preservation of these cells in order to find therapies for a variety of diseases. Stem cells will most likely be widely used in clinical trials and therefore, as proposed by Kimmelman and other authors,⁵⁶ there is a sound rationale for supporting the call for the establishment of mandatory international clinical trial registries for stem cell-based research.⁵⁷ A clinical trials registry (CTR) for stem cell-based research could follow the model established by other international CTRs, such as those for human gene transfer.⁵⁸

Stem cell clinical trial registries will provide the public with complete and accurate information regarding stem cell therapies so that they too can participate meaningfully in policy discussions regarding this scientific field. These registries will also highlight any negative trial outcomes, allowing policy-makers to quickly identify and address safety concerns in stem cell research. For both scientific and pragmatic reasons, these stem cell CTRs should be part of a widely recognized stem cell bank such as the United Kingdom Stem Cell Bank,⁵⁹ the ISCF registry, or the ISSCR stem cell bank.

The time is ripe to move the debate from the appropriateness of registration and publication of clinical trials,⁶⁰ and from the suitability of a CTR for stem cell-based research, to the issue of how to organize such a clinical trial registry in a sound, efficient and transparent fashion for the public good.⁶¹

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Figure 8: Stem Cell Banks in Existence or Development

<p><i>International Stem Cell Forum (ISCF)</i> http://www.stemcellforum.org/</p>	<p>The ISCF is in the process of developing an international registry to record quality stem cell lines. The main objective is to coordinate stem cell banking in different countries and to promote the standardization of procedures in this field of research.</p>
<p><i>International Society for Stem Cell Research (ISSCR)</i> http://www.isscr.org/</p>	<p>The ISSCR proposes to maintain a database of human stem cell lines and will give the ISSCR Standards Committee the mandate to verify the provenance of the stem cell lines according to guidelines established by the ISSCR.</p>
<p><i>National Institute of Health (NIH)</i> (United States) http://stemcells.nih.gov/research/registry/defaultpage.asp</p>	<p>National Stem Cell Bank (developed by the WiCell Research Institute) will provide stem cells to researchers from federally funded organizations at a reduced price. It is ensured that the stem cell lines and classes are properly maintained and handled. The bank houses 11 of the 22 stem cell lines that exist in the United States. Each stem cell line has a unique NIH code for identification.</p>
<p><i>European Registry for hESC lines</i> http://europa.eu/rapid/pressReleasesAction.do?reference=IP/07/437&format=HTML&aged=0&language=EN&guiLanguage=en</p>	<p>On March 29, 2007, the European Commission decided to provide funding for the creation of a European hESC line registry. The registry will be publicly accessible via the internet, will contain information regarding stem cell lines (provenance, contact information, cell characteristics) and will also provide information regarding developments in stem cell research, such as clinical trials. Ten EU countries are currently involved in the registry and it is expected that other non-EU countries will join the project.</p>
<p><i>UK Stem Cell Bank</i> (United Kingdom) http://www.ukstemcellbank.org.uk/</p>	<p>A repository of human stem cells of all types. The bank is governed by strict guidelines to ensure the highest standards of best practice regarding human stem cell use.⁵⁴</p>
<p><i>Canadian Institutes of Health Research (CIHR)</i> (Canada) http://www.cihr-irsc.gc.ca/</p>	<p>In their <i>Updated Guidelines for Human Pluripotent Stem Cell Research</i>,⁵⁵ the CIHR proposed the creation of a national registry for stem cell banks (Section 6.0).</p>

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