23 September, 2006

Senate Standing Committee on Community Affairs
Australian Senate

Re: Legislative Response to Recommendations of the Lockhart Review

Dear Committee Members,

Thank you for opportunity to make a submission regarding the legislative response to the recommendations of the Legislative Review Committee on the *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* (the Lockhart Review).

Stem Cell Sciences Ltd is the Australian operation of the global biotechnology company, Stem Cell Sciences (AIM:STEM), which is focused on the provision of stem cells and technology for biopharmaceutical research and clinical applications.

As a major stakeholder in the stem cell field, Stem Cell Sciences has been actively involved in the Lockhart Review lodging a written submission (Submission 318) and appearing before the Committee during their Melbourne consultation at both a private meeting, site visit and the public facilitated discussion forum. Our participation is reflected by numerous citations in the Lockhart Review Committee Reports.

Stem Cell Sciences believes that the Lockhart Review was conducted with great sensitivity and diligence, involving extensive consultation with the public and stakeholders. We support all of the 54 Lockhart Recommendations and believe it would be a great pity if the Committee's well reasoned recommendations are ignored.

The current Australian legislation should be amended to enable responsible, regulated research using human embryos to continue and progress in Australia - as recommended by the Lockhart Review - bringing us into line with other forward looking countries. As such we welcome the draft *Somatic Cell Nuclear Transfer and Related Research Amendment Bill 2006* from Senators Stott Despoja and Webber and look forward to a future Bill from Senator Patterson.

Stem Cell Sciences would very much like to appear before the Senate Committee during its public hearings in Melbourne on 24 October 2006 to discuss our support of the Lockhart recommendations especially in relation to significant advances in the stem cell field that justifies the continuing use of human embryos in research and an extension to allow the derivation of human stem cell lines through the use of somatic cell nuclear transfer (SCNT).

As a Company actively exploring the therapeutic potential of different stem cell types, including both adult and embryonic stem cells, we believe that it is not yet clear which stem cell type will be of most value in certain therapeutic indications and that both must be pursued in order to deliver the most effective and safest medical outcomes. The debate surrounding the Lockhart Review recommendations should not be about which type of stem cell is superior but about how to regulate valuable and necessary research to advance regenerative medicine in Australia.

We have included below a brief summary that highlights some of the notable publications since 2002 for your consideration.

The views stated above are shared by senior management at Stem Cell Sciences Ltd.

Yours sincerely,

Mr David Newton
General Manager
Stem Cell Sciences Ltd

Registered Office:
1st Floor, 28 Riddell Parade
Elsternwick Victoria 3185
Australia

Telephone: +61 3 9905 0601
Facsimile: +61 3 9824 6031

Laboratories:
P.O. Box 8224
Monash University L.P.O.
Clayton Victoria 3168
Australia
Telephone: +61 3 9905 0600
Facsimile: +61 3 9905 0611

ADVANCES IN HUMAN EMBRYONIC STEM CELL RESEARCH SINCE 2002

In summary, since 2002 there have been several major publications that demonstrate the advances in human embryonic stem cell research. These include:

- Improvements in the quality of embryonic stem cell lines towards generation of cells that could be used for a clinical application[1, 2,3];
- Numerous examples of differentiation and engraftment of cells derived from human and animal embryonic stem cells in animal models[4,5,6,7,8, 9,10,11];
- Correction of genetic abnormalities in mouse embryonic stem cells[12,13];
- Value of embryonic stem cells in drug screening and toxicology[14,15,16,17];
- Demonstration that stem cells generated from SCNT share the same characteristics as those derived from a fertilised blastocyst in animal models[18, 19];
- Basic proof-of-concept that stem cells generated by SCNT could partially restore function in animal models[13,20];
- Value of SCNT to investigate epigenetic factors including cancer characteristics in animal models[21,22].

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[1] Ludwig T et al (2006). Derivation of human embryonic stem cells in defined conditions. Nature Biotechnol. 24: 185 – 187.

[2] Liu Y et al (2006). A novel chemical-defined medium with bFGF and N2B27 supplements supports undifferentiated growth in human embryonic stem cells. Biochem. Biophys. Res. Comm. 346: 131 – 139.

[3] Ellerström et al (2006). Derivation of xeno-free human ES cell line. Stem Cells (published on-line June 1 2006).

[4] Trounson (2006). The production and directed differentiation of human embryonic stem cells. Endocrine Rev 27: 208 – 219.

[5] Ben-Hur et al (2004). Transplantation of human embryonic stem cell-derived neural progenitors improves behavioral deficit in Parkinsonian rats. Stem Cells 22: 1246 - 1255.

[6] Takagi et al (2005). Dopaminergic neurons generated from monkey embryonic stem cells function in a Parkinson primate model. J Clin Invest 115: 102 – 109.

[7] Kehat et al (2004). Electromechanical integration of cardiomyocytes derived from human embryonic stem cells. Nature Biotech 22: 1282 - 1289.

[8] Faulkner and Keirstead (2005). Human embryonic stem cell-derived oligodendrocyte progenitors for the treatment of spinal cord injury. Transpl Immunol. 15: 131 - 142.

[9] Keirstead et al (2006). Human embryonic stem cell-derived oligodendrocyte progenitor cell transplants remyelinate and restore locomotion after spinal cord injury. J. Neurosci. 25 : 4694 – 4705.

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[11] Zheng et al (2006). Skeletal myogenesis by embryonic stem cells. Cell Res 16: 713 – 722.

[12] Chang et al (2006). Correction of the sickle cell mutation in embryonic stem cells. Proc Natl Acad Sci USA 103: 1036 – 1040.

[13] Rideout et al (2002). Correction of a genetic defect by nuclear transplantation and combined cell and gene therapy. Cell 109: 17 - 27.

[14] Gorba and Allsopp (2003). Pharmacological potential of embryonic stem cells. Pharmacol Res 47: 269 - 278.

[15] Davila et al (2004). Use and application of stem cells in toxicology. Toxicol Sci 79: 214 – 223.

[16] Gorba and Allsopp (2003). Pharmacological potential of embryonic stem cells. Pharmacol Res 47: 269 - 278.

[17] Kulkarni and Khanna (2006). Functional hepatocyte-like cells derived fropm mouse embryonic stem cells: a novel in vitro hepatotoxicity modle for drug screening. Toxicology In Vitro 20: 1014 – 1022.

[18] Brambrink et al (2006). ES cells derived from cloned and fertilized blastocysts are transcriptionally and functionally indistinguishable. Proc. Natl. Acad. Sci. USA 103: 933 – 938.

[19] Wakayama et al (2006). Equivalency of nuclear transfer-derived embryonic stem cells to those derived from fertilized mouse blastocysts. Stem Cells 24: 2023 – 2033.

[20] Barberi et al (2003). Neural subtype specification of fertilization and nuclear transfer embryonic stem cells and application in parkinsonian mice. Nature Biotech 21: 1200 – 1207.

[21] Blelloch et al (2004). Nuclear cloning of embryonal carcinoma cells. Proc Natl Acad Sci USA 39: 13985 – 13990.

[22] Hochedlinger et al (2004). Reprogramming of a melanoma genome by nuclear transplantation. Genes and Dev 18: 1875 – 1885.

It should also be stated since our submission last year, the previous claims that human stem cell lines made by a group in South Korea have been derived using SCNT have been shown to be fraudulent and retracted[23].

To date no human stem cell lines have been generated using SCNT[24,25]. However, there are now several groups in the UK and USA actively attempting to perform SCNT for stem cell derivation using human cells under supportive regulatory frameworks[26,27,28,29].

Since 2002, there have been several publications reporting the development of alternative ways of generating stem cells through use of animal eggs[30], fusion to pluripotent cells[31] or induced changes in gene expression[32].

While these approaches may one day replace the need for human eggs to generate "tailored" stem cell lines, currently each approach has a significant limitation. At present the best approach to generate patient or disease-specific stem cell lines for research and therapeutic applications remains through the use of SCNT using human eggs.

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[24] Stojkovic et al (2005). Derivation of a human blastocyst after heterologous nuclear transfer to donated oocytes. Reproductive BioMedicine Online 11: 226 - 231.

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[32] Takahashi and Yamanaka (2006). Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell 126: 663 – 676.