

ISSUES IN MEDICINE

**Regulatory crackdown on stem cell therapy:
What would the position be in South Africa?**

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This article attempts to answer the question of whether stem cell therapy falls within the current South African regulatory framework, using the Regenexx case in the USA as an example. The USA regulator, the Federal Drug Administration (FDA), is seeking to regulate the Regenexx autologous stem cell therapy as a 'drug' and a 'biological product'. The opposing position taken by the inventors of the Regenexx therapy is that re-implantation of one's own body parts can in principle not be a 'drug' and that the FDA is exceeding its mandate. In this article arguments are presented that the Regenexx therapy would qualify as a 'biological medicinal product' in the South African regulatory framework established in terms of the Medicines and Related Substances Control Act. As such, the Regenexx therapy

would be subject to registration with the Medicines Control Council (MCC) as a legal precondition for its commercialisation. Furthermore, in order to convince the MCC of the safety, efficacy and quality of the Regenexx therapy, such therapy must – similar to any other new medicine – first be subjected to clinical trials. It is therefore concluded that stem cell therapy is indeed comprehensively regulated in South Africa, and that a recent opinion expressed in this journal that there exists a 'legislative vacuum' with relation to the regulation of stem cell therapy in South Africa is plainly incorrect.

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As biomedical technology regarding stem cells moves rapidly ahead, new challenges to the existing regulatory frameworks will arise. Such a challenge by Regenerative Sciences Inc in the USA recently culminated in the filing of a lawsuit by their regulator, the Food and Drug Administration (FDA). This lawsuit may last for years. Each opposing side bases its case on well-articulated legal values. The USA court decision in this case will reverberate worldwide and may be cited in future South African constitutional jurisprudence. The relevance of each side's arguments in this matter in the South African legal context is evaluated and an outcome ventured should a similar case be filed in South Africa today.

The facts of the matter¹

Regenerative Sciences pioneered a stem cell therapy for orthopaedic problems, marketed under the trademark 'Regenexx'. It entails harvesting a patient's own bone marrow or synovial fluid surrounding the joints. Stem cells isolated from this tissue are grown, processed, mixed with medicinal products outside the body and injected back into the patient. Regenerative Sciences claims that this assists to regenerate bone and cartilage. They published a study involving 227 patients and are submitting another study with 339 patients. Both studies show that this novel stem cell-based procedure is dramatically safer than the more invasive surgical procedures which it helps many patients avoid. However, these studies did not include the scientific controls usually expected of clinical trials for new medicines.

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Overview of arguments

The FDA's position is that the autologous stem cell-based substance produced using the Regenexx procedure ('the Regenexx stem cells') is a 'biological product' and since therapeutic claims are made about the Regenexx stem cells, they also qualify as a 'drug' and accordingly fall within their regulatory mandate.²

Regenerative Sciences' position is that the FDA is acting *ultra vires*, arguing that the FDA's mandate is to regulate 'one-on-many' public health risks (e.g. mass production of drugs by a pharmaceutical company), and not 'one-on-one' doctor-patient medical care risks. As the Regenexx stem cells are autologous, therapy amounts to the implantation of the patient's own tissue and falls within the 'one-on-one' category. Therefore the FDA has no authority to regulate the Regenexx stem cells.³

Analysis of arguments

Would the Regenexx stem cells be subject to regulation in South Africa?

The nature of the Regenexx stem cells in the South African medicolegal context

The legal framework to introduce a new therapeutic substance to the South African market is established primarily by the Medicines and Related Substances Control Act⁴ ('the Medicines Act'). Whether the Regenexx stem cells would fit into this legal framework will depend on whether they qualify as 'medicine' in terms of the Medicines Act – 'medicine' being South Africa's equivalent legal term for 'drug' in the USA. If the Regenexx stem cells qualify as medicine, the degree of regulation will depend on whether the Regenexx stem cells have been called up for registration by a notice in terms of the Medicines Act.

The definition of 'medicine' in the Medicines Act is broad: 'medicine' means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in: (i) the diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in man; or (ii) restoring, correcting or modifying any somatic or psychic or organic function in man.

It is clear that the Regenexx stem cells would qualify as a medicine as they are a substance, have mass and occupy space, and purport to be suitable for a therapeutic use.

More specifically, the Regenexx stem cells would be classified and regulated as a 'biological medicinal product'. The Medicines Control Council (MCC), the regulatory body established by the Medicines Act, has published guidelines regarding good manufacturing practice,⁵ and guidelines to assist prospective introducers of new substances that may qualify as medicines.⁶ These define 'biological medicinal products' as including medicines that are 'derived or extracted from biological tissue'.⁷ Since the Regenexx stem cells are derived from a patient's tissue, they fit the definition neatly. An official notice by the MCC states that all medicines that are 'biological products' (i.e. biological medicinal products) must be registered with the MCC and are listed as scheduled substances under Category A, Classification 30.⁸ Thus, the Regenexx stem cells would have to be registered with the MCC.

What about Regenerative Sciences' *ultra vires* argument?

Unlike in the USA, South African law does not distinguish between 'one-on-one' and 'one-on-many' risk. The Supreme Court of Appeal ruled that to exempt a subsection of the population (in this analysis patients who wish to use individualised 'one-on-one' stem cell therapy) from the provisions of the Medicines Act – even if such subsection of the population *wants* to be exempted! – would undermine the purpose of the Medicines Act to protect the *entire* population and therefore cannot be allowed.⁹ South African courts have consistently given a broad interpretation to the MCC's mandate.¹⁰

Does the fact that Regenexx stem cells are human body parts not exclude them from qualifying as medicine? As the Medicines Act provides no such exclusion, there is no basis for such a mutually exclusive alternatives-paradigm. The Regenexx stem cells qualify as medicine, irrespective of their characteristics that are irrelevant to the definition of 'medicine', such as being human body parts or being transplanted/implanted.

Therefore I must conclude that the chances of success of Regenerative Sciences' *ultra vires* argument would be weak.

How would the Regenexx procedure be regulated in South Africa?

The effect of the Regenexx stem cells qualifying as registrable medicine is that they may only be supplied to a patient *if* the MCC is satisfied with their safety, efficacy and quality and hence grants their registration. The MCC may also make registration subject to certain conditions. General conditions, such as those regarding good manufacturing practice for biological medicinal products, would apply to the Regenexx procedure.

To convince the MCC of the safety, efficacy and quality of a new medicine, an applicant will be expected to have conducted well-constructed and controlled clinical trials.¹¹ The MCC regulates this to protect human subjects, and requires prior permission and regular reporting.

A complementary statute that will also affect the Regenexx process is the Human Tissue Act.¹² Since human tissue is harvested for 'the production of a therapeutic substance', such harvesting and the subsequent isolation of stem cells, cryopreservation and preparation

of the therapeutic substance are legal. This is subject to provisions, including: harvesting must be done by or under supervision of a medical practitioner; the patient must give informed consent; and the isolation of stem cells, cryopreservation and preparation of the therapeutic substance must take place in an authorised institution.

Conclusion and rectifying the perception of a 'regulatory vacuum'

I conclude that all aspects of the Regenexx process would be legally regulated in South Africa, contrary to statements that stem cell therapy is in a 'regulatory vacuum' in South Africa.¹³ That paper highlights the problem of the proliferation of untested 'stem cell therapies' around the world and advocates an ethical stance to protect the public from potential abuses; any person of conscience must agree with this position; and South Africa is sketched as attractive for companies looking for a slack stem cell therapy regulatory regimen. I strongly differ from this opinion and as indicated, using Regenexx as a test case, new stem cell therapies would be subject to the same safety, efficacy and quality requirements as any other new medicine. The paper states: 'Chapter 8 of the National Health Act (the major part of the legislation in South Africa that deals with the issue of cell-based therapy) has not been promulgated. This is a serious hiatus, since we have to rely on the outdated Human Tissue Act of 1983 to provide the necessary legislation.'¹³

The reason for the conclusion that there exists a 'legislative vacuum' in South Africa is the failure to take cognisance of the Medicines Act, which is the primary legislation that regulates cell-based therapy, and the failure to consider any relevant case law.

The public must be protected against unethical medical practices. However, making the right legal diagnosis is the essential first step to addressing social ills and averting the potential proliferation of untested 'stem-cell therapies'.

1. Eisner W. 'FDA Hauls Regenexx Into Court.' Orthopedics This Week. 18 August 2010. http://ryortho.com/fda.php?news=686_FDA-Hauls-Regenexx-Into-Court (accessed 20 December 2011).
2. FDA. Letter to Regenerative Sciences, Inc. 25 July 2008. <http://www.docstoc.com/docs/1046270/FDA-Untitled-Letter-to-Regenexx-%28Regenerative-Sciences-Inc---RSI%29> (accessed 20 December 2011).
3. Centeno CJ. Should autologous stem cells be regulated the same as mass produced drugs? (Abstract of a presentation to the Tissue Engineering and Regenerative Medicine Society, December 2010.) <http://www.regenexx.com/tag/fda/> (accessed 20 December 2011).
4. Act 101 of 1965.
5. MCC. Guidance Document: Good Manufacturing Practice for Medicines in South Africa. Pretoria: Government Gazette, 2 May 2003.
6. MCC. General Information document for human medicines. http://www.mccza.com/dynamism/default_dynamic.asp?grpID=28&doc=dynamic_generated_page.asp&catID=172&groupID=28 (accessed 20 December 2011).
7. Note that the terms 'biological', 'biological medicinal product' and 'biological medicine' are used interchangeably in the Guidance Document: Good Manufacturing Practice for Medicines in South Africa. The General Information document consistently employs the term 'biological medicine'.
8. Notice in terms of s14(2) of the Medicines Act published in the Government Gazette of 21 September 1984.
9. Prince v President of the Law Society of the Cape of Good Hope and Others 2000 (3) SA 845 (SCA); 2000 (7) BCLR 823 (SCA) para 12.
10. See for example: Reitzer Pharmaceuticals (Pty) Ltd v Registrar of Medicines and Another 1998 (4) SA 660 (T); Treatment Action Campaign and Another v Rath and Others [2008] ZAWCHC 34; [2008] 4 All SA 360 (C).
11. MCC. Registration of Medicines: General Information. Accessible online at: http://www.mccza.com/genericDocuments/2.01_General_information_Mar11_v7_track_changes.doc (accessed 20 December 2011).
12. Act 65 of 1983.
13. Pepper MS. 'Cell-based therapy – navigating troubled waters' S Afr Med J 2010;100:286-288.

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