A review of the newer progressive worldwide regulations for cellular therapy

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Abstract

Despite significant basic research and substantial clinical evidence of safety and efficacy of cellular therapy over the last 20 years, cellular therapy has still not become a standard of care in Neurorestoratology. This has been primarily due to restrictive regulatory systems worldwide. The current regulatory systems have evolved over the past 50 years primarily to regulate drugs and medical products. Cells are not drugs and therefore, regulations for drugs cannot be extrapolated to cells. In the year 2001, President of the USA, George W. Bush restricted federal funding for research on human embryonic stem cells. This ban negatively affected all of medical thinking for all forms of cellular therapy including other cell types which are low risk and less controversial such as adult stem cells. This is particularly unfortunate as safer forms of cellular therapy have the potential to help patients suffering with incurable medical conditions that cause death and disability. Realizing this several countries are now coming up with newer laws and regulations for cellular therapy. The common aspects of these new regulations are (a) Realization of the need for fast track approval for cellular therapy (b) To distinguish between cellular therapy products and cellular therapy procedures (c) To have more permissive regulations for the lower risk cell therapies which are mainly the autologous and minimally manipulated cell therapies (d) Need to have more permissive regulations for on compassionate grounds for conditions that are incurable and cause death or disability. Examples of such new regulations are from countries like Japan, Korea, USA, India and Australia. **Japan:** In 2014, Japan passed two separate laws for stem cell products and stem cell procedures. Pharmaceutical, medical devices and therapeutic products Act (PMDA) which is the Revised Pharmaceutical Affairs act deals with licensing of regenerative medical products and, Act on Safety of Regenerative Medicine (ASRM) deals with standards for institutions providing regenerative medicine and cell culturing and processing facilities. This law makes a distinction between low, medium and high-risk regenerative medicines. For low risk cellular therapy an approval is required only from an institutional committee. **Korea:** The Korean Regulations have also excluded minimally manipulated cells from their 'Review and authorization of Bio logical products' in view of low risk profile.**USA:** (a) **Charlie's law:** State of Texas passed Charlie's law in May 2017 which was specifically designed for adult stem cells; allowing patients with severe chronic or incurable diseases access to experimental stem cell treatments. According to this law, if the standard treatment options are unavailable or unlikely to alleviate the significant impairment or severe pain associated with the severe chronic disease or terminal illness, the treating physician can prescribe or recommend in writing, use of a specific class of investigational stem cell treatment. The treatment should be administered by a certified physician, in a licensed

medical hospital/ college and should be overseen by an institutional review board (b) **Right to Try Act** was passed by USA federal government in May 2018 with the intent of allowing terminally ill patients access to experimental therapies on a case by case review basis. Although this is not designed specifically for cell therapy it includes cell therapy along with other unproven treatments. **Australia:** Therapeutic goods administration (TGA), Department of Health, Australia has exempted low risk autologous stem cell treatments collected by a qualified treating doctor in the registered hospital premise; from regulation by TGA. **India:** For the last several years India had very restrictive guidelines for stem cell research. However, in the past two years the health ministry along with the CDSCO has started adopting a more realistic approach. In March 2019, Ministry of Health and Family Welfare, included "stem cell derived products" in the definition of a "new drug". The government had earlier defined Stem Cell and Cell based Products as those which have been derived from processed cells including cell or tissue which has been processed by means of substantial or more than minimal manipulation. By doing so stem cell products were separated from procedures and minimally manipulated non processed autologous cells were being kept out of the regulatory restrictions.

Regulatory bodies the world over have been reluctant to let go of the bureaucratic controls they have been exercising so far. It is therefore important the Government leaders seize the initiative and take executive decisions and frame new laws to overrule the bureaucracy and thereby ensure that the millions of dying and disabled patients in their countries have easier access to cellular therapy. Several other countries are now working to come up with more permissive regulations. In conclusion all laws / regulations for cellular therapy should be based on the following principles:

A] Regulations should distinguish between cell therapy products and medical procedures. Whereas cell products manufactured commercially need to be highly regulated, cellular procedures done by doctors in their hospitals as part of their medical practice need to have permissive regulations.

B] Low risk cellular therapies such as Autologous minimally manipulated should be permitted for clinical use if a) A qualified doctor is performing the procedure, b)The hospital in which the procedure is being performed is registered with local governing bodies, c)Informed consent is taken from the patient and d)Institutional Ethics Committee has approved the protocol of therapy C] Regulations should be more permissive for compassionate use of cellular therapy in conditions that cause death and disability.