SECOND POSITION PAPER OF THE PROFESSIONAL REGULATORY BOARD OF MEDICINE ON STEM CELL THERAPY AND RELATED CONCERNS

The Professional Regulation Commission and the Professional Regulatory Board of Medicine constitute the regulatory body for the practice of medicine in the country, As part of their regulatory functions with quasi-judicial and quasi-legislative powers, they hereby issue the following statements on matters dealing with the competencies of specialists, the practice of stem cell therapy, the principle of innovative therapy, and the SEC registration of PSSCM.

At the outset, the following delineation of authority should be made clear:

a. The government regulatory body for the practice of medicine: Professional Regulation Commission (PRC) and the Professional Regulatory Board of Medicine (PRBOM). The PRC/PRBOM license physicians and regulate the practice of the profession.

b. The government regulatory body for hospitals, clinics and laboratories: Department of Health (DOH). The DOH licenses hospitals, clinics and laboratories.

c. The government regulatory body for drugs and stem cell solutions/products: Food and Drug Administration (FDA). The FDA licenses the use of drugs, stem cell products and solutions.

Main consideration: Patient Safety

The International Association of Medical Regulatory Authorities (IAMRA) lists the Board of Medicine as the regulatory authority in the Philippines. The ASEAN MRA for Medical Practitioners included the Professional Regulation Commission and the Professional Regulatory Board of Medicine as the Professional Regulatory Authorities (PRA) for the Philippines

The PRBOM agrees with the IAMRA declaration that the mandate of medical regulatory authorities is **to protect, promote and maintain the health and safety of the public by ensuring proper standards for the profession of medicine.**

For the protection of the public, the PRBOM hereby defines the Quality Standards for specialists most qualified and most competent to practice and to conduct research in stem cell therapy.

I. **QUALITY STANDARDS FOR SPECIALISTS TO PRACTICE STEM CELL THERAPY FOR PROVEN INDICATIONS (Based on US FDA)**

For proven indications, the PRBOM mandates that based on the disorders/diseases, the appropriate specialists, based on education, training, clinical experience and certification, to perform treatment are the following:

1. Bone marrow transplantation for hematologic disorders/diseases: Diplomates and Fellows of the Philippine Society of Hematology and Blood Transfusion, Philippine Society of Pediatric Hematology (PSPH).
2. Corneal resurfacing with limbal stem cells for ocular disorders/diseases: Diplomates and Fellows of the Philippine Academy of Ophthalmology.

II. **QUALITY STANDARDS FOR SPECIALISTS TO CONDUCT CLINICAL TRIALS IN STEM CELL THERAPY FOR UNPROVEN INDICATIONS (Based on US FDA)**

For unproven indications, the PRBOM mandates that based on the disorders/diseases, the appropriate specialists (based on education, training, clinical experience and certification) to conduct clinical trials are the following:

1. For musculoskeletal disorders/diseases: Diplomates and Fellows of the Philippine Orthopedic Association and the College of Rheumatology.
2. For eye disorders/diseases: Diplomates and Fellows of the Philippine Academy of Ophthalmology.
3. For heart disorders/diseases: Diplomates and Fellows of the Philipppine College of Cardiology / Pediatric Cardiology and cardiac surgeons from the Philippine Association of Thoracic and Cardiovascular Surgeons.
4. For neurologic disorders/diseases: Diplomates and Fellows of the Philippine Neurology Association / Pediatric Neurology and Association of Filipino Neurosurgeons.
5. For pulmonary disorders/diseases: Diplomates and Fellows of the Philippine College of Chest Physicians and thoracic surgeons from the Philippine Association of Thoracic and Cardiovascular Surgeons.
6. For renal and urologic disorders/diseases: Diplomates and Fellows of the Philippine Society of Nephrology and Philippine Urological Association.
7. For autism: Diplomates and Fellows of the Philippine Pediatric Society, Philippine Society for Developmental and Behavioral Pediatrics (PSDBP).
8. For gynecologic disorders/diseases: Diplomates and Fellows of the Philippine Obstetrical and Gynecological Society.
9. For aging disorders/diseases: Diplomates and Fellows of the Geriatric Society
10. For malignant diseases: Diplomates and Fellows of the Philippine Society for Medical Oncology

III. THE PRINCIPLE OF INNOVATIVE THERAPY

The discussion whether a certain kind of treatment is innovative therapy or a research undertaking has been going for some time. The distinguishing feature is the intent, meaning when the physician has the intention of gathering data in order to produce generalizable knowledge meant to be shared with others, then it falls under research. This would then need strict regulation and approval from Institutional Research or Review Boards (IRB's) or Ethics Committees.

Classifying stem cell therapy as innovative therapy implies that it is outside the authority of the government regulatory bodies. It does not pass the scrutiny, approval and monitoring of Institutional Review Boards or Ethics Committees. Ascertaining the safety of patients will only depend on the professional responsibility of the physician implementing the treatment. The problem lies in the fact that so many unscrupulous physicians have been misrepresenting themselves as experts in this field already. Classifying this as innovative therapy will lead to a situation where anybody declaring an "Interest" in stem cell therapy will be allowed to practice it. The absence of regulation will subject many patients to unnecessary risks and hazards.

The Professional Regulatory Board of Medicine declares and asserts that if the members of any stem cell society and other physicians maintain that stem cell therapy is classified as innovative therapy, they will still have to contend with the requirement that only physicians who have acquired the education, training, and certification in the field of stem cell therapy are allowed to implement an innovative therapy. If the physicians attempting to provide stem cell therapy have not acquired basic training and certification, then they should be subjected to strict requirements set by the regulatory body for the practice of medicine in the country.

Every physician is required to have a record of every patient seen or treated detailing the presenting problems, clinical history, physical examination findings, diagnostic tests and results, treatment implemented, drugs administered, procedures performed, and results of treatment based on long term follow up and monitoring. There should be no hesitation in sharing the results of a scientific study with the rest of the medical community. All physicians should be familiar with the levels of evidence when it comes to research. Physicians should stop using anecdotes and testimonials from selected patients in promoting products and procedures that they themselves are endorsing. Anecdotes and testimonials are not accepted as the most reliable evidence of whether a treatment is effective. Objectivity and integrity should always be maintained. This is what professionalism and ethics in the practice of medicine dictate.

IV. THE CONDUCT OF CLINICAL TRIALS

The Professional Regulatory Board of Medicine is adopting the **International Society for Stem Cell Research (ISSCR)** recommendations, as follows:

Recommendation 21: (Re general conduct of stem cell treatments)

All studies involving clinical applications of stem cells, whether publicly or privately sponsored, must be subject to independent review, approval, and ongoing monitoring by human subjects research oversight bodies with supplemental appropriate expertise to evaluate the unique aspects of stem cell research and its application in a variety of clinical disciplines. This review and oversight process must be independent of the investigators regardless of whether it occurs at the institutional, regional, or national level, and regardless of whether investigators employ the services of a contract research organization.

Recommendation 23: (Peer Review Process)

The peer review process for stem cell-based clinical trials should have appropriate expertise to evaluate (a) the in vitro and in vivo preclinical studies that form the basis for proceeding to a clinical trial and (b) the scientific underpinnings of the trial protocol, the adequacy of planned end-points of analysis, statistical considerations, and disease-specific issues related to human subject protection.

Recommendation 26: (Comparison of stem cell treatments to current standard of care)

Clinical research should compare new stem cell-based therapies against the best medical therapy currently available to the local population.

Recommendation 28: (Re Patient Informed Consent)

Informed consent is particularly challenging for clinical trials involving highly innovative interventions.

(a) Patients need to be informed when novel stem cell-derived products have never been tested before in humans and that researchers do not know whether they will work as hoped.

(b) Cell-based interventions, unlike many pharmacological products or even many implantable medical devices, may not leave the body and may continue to generate adverse effects for the lifetime of the patient. The possible irreversibility of a cellular transplant should be explained clearly.

(c) Subjects should be informed about the source of the cells so that their values are respected.

(d) Ensuring subject comprehension must be done at each phase of the clinical trials process. Ideally, the subject's comprehension of information should be assessed through a written test or an oral quiz during the time of obtaining consent.

(e) Human subjects research committees should ensure that informed consent documents accurately portray these uncertainties and potential risks, and clearly explain the experimental nature of the clinical study.

Recommendation 33: (Publication of both positive and negative results of treatment)

Researchers should publish both positive and negative results and adverse events. To ensure the integrity of scientific information and to promote the highest standards of professional conduct, researchers should present their results at professional scientific conferences or in peer-reviewed scientific journals before reporting their research to the lay media or to patient ++advocacy groups and associations.

Recommendation 34: (Stem cell treatments outside clinical trials or "humanitarian"clause)

Clinician-scientists may provide unproven stem cell-based interventions to at most a very small number of patients outside the context of a formal clinical trial, provided that:

(a) There is a written plan for the procedure that includes:

i. scientific rationale and justification explaining why the procedure has a reasonable chance of success, including any preclinical evidence of proof-of-principle for efficacy and safety;

ii. explanation of why the proposed stem cell-based intervention should be attempted compared to existing treatments;

iii. full characterization of the types of cells being transplanted and their characteristics as discussed in Section 4, Cell Processing and Manufacture;

iv. description of how the cells will be administered, including adjuvant drugs, agents, and surgical procedures; and

v. plan for clinical follow-up and data collection to assess the effectiveness and adverse effects of the cell therapy;

(b) the written plan is approved through a peer review process by appropriate experts who have no vested interest in the proposed procedure;

(c) the clinical and administrative leadership supports the decision to attempt the medical innovation and the institution is held accountable for the innovative procedure;

(d) all personnel have appropriate qualifications and the institution where the procedure will be carried out has appropriate facilities and processes of peer review and clinical quality control monitoring;

(e) voluntary informed consent is provided by patients who appreciate that the intervention is unproven and who demonstrate their understanding of the risks and benefits of the procedure;

(f) there is an action plan for adverse events that includes timely and adequate medical care and if necessary psychological support services;

(g) insurance coverage or other appropriate financial or medical resources are available to patients to cover any complications arising from the procedure; and

(h) there is a commitment by clinician-scientists to use their experience with individual patients to contribute to generalizable knowledge. This includes:

i. ascertaining outcomes in a systematic and objective manner;

ii. a plan for communicating outcomes, including negative outcomes and adverse events, to the scientific community to enable critical review (for example, as abstracts to professional meetings or publications in peer-reviewed journals); and

iii. moving to a formal clinical trial in a timely manner after experience with at most a few patients.

This second position paper on stem cell therapy and related concerns is issued to provide information and guidance to the public, and to all members of the medical profession.

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