[DOH ADMINISTRATIVE ORDER NO. 2013-0012, March 18, 2013]

RULES AND REGULATIONS GOVERNING THE ACCREDITATION OF HEALTH FACILITIES ENGAGING IN HUMAN STEM CELL AND CELL-BASED OR CELLULAR THERAPIES IN THE PHILIPPINES

I. RATIONALE/BACKGROUND

Stem cells science and technology is considered the future of medicine. The government encourages that various stakeholders participate in the development of the science of stem cell therapy. But as with any new technology or innovation, there is a need for regulatory oversight that will provide protection to the public. It is also necessary to inform the public of this new technology of its potential benefits and risks.

Stem cells are unspecialized cells capable of renewing themselves and differentiating into other cell types, even after long periods of inactivity. Under certain physiologic or experimental conditions, they can be induced to become tissue-or organ-specific cells with special functions. In some organs such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide, only ivied under special complex conditions.

Stem cell-based therapies have existed for the past four decades. There are stem cell-based therapies, which have been proven to be effective in some medical conditions such as some forms of blood dyscracias. Stem cells that come from the bone marrow or blood have already been routinely used in transplant procedures to treat patients with cancer and other disorders of the blood and immune system.

The rapid development of techniques to grow human stem cells in culture coupled with an increased understanding of cell differentiation have expanded its promising therapeutic uses for diseases such as spinal cord injury, stroke, autism, Parkinson's disease, and others. However, stem cell treatments offered today are a type of cell therapy that introduce new cells into adult bodies for possible treatment of cancer, diabetes, neurological, and other conditions with the latest passion for skin rejuvenation or aesthetic purposes. This is becoming a significant item of interest and concern within the media, the internet and our society, as some clinics and providers claim success in treating patients but few has published data from controlled clinical trials.

In a recent study conducted by the Bureau of Health Facilities and Services (BHFS) of the Department of Health (DOH) pursuant to Department Memorandum No. 2011-0135 entitled "A Survey of the Services and Equipment Available in Hospitals Nationwide", the findings revealed that five (5) hospitals and some ambulatory surgical clinics were providing stem cell services to patients for various indications.

Given the recent developments in stem cell and cell-based research and therapy, the Department of Health sees it imperative to develop and strengthen the regulatory framework to ensure access to safe and quality health facilities engaging in human stem cell and cell-based or cellular therapies in the Philippines.

II. OBJECTIVE

These rules and regulations are promulgated to protect the public and assure the safety of patients and personnel by:

A. Preventing the introduction, transmission and spread of communicable diseases by ensuring as minimum quality of service rendered by hospitals and other health facilities engaging in human stem cell and cell-based therapies; and
B. Ensuring that human stem cell and cell-based therapies are safe and effective for their intended use.

III. SCOPE

These rules and regulations shall apply to all government and private facilities that are and will be involved in the use of human stem cell and cell-based or cellular therapies.

IV. TERMINOLOGY, ABBREVIATIONS AND DEFINITIONS

For the purposes of this order, the following terms, abbreviations and definitions apply:

1. *Adverse Reaction* – any unintended or unfavorable sign, symptom, abnormality, or condition temporarily associated with an intervention that may or may not have a causal relationship with the intervention, medical treatment, or procedure. Adverse reaction is a type of adverse event.
2. *Adverse Event* - a noxious and unintended response suspected or demonstrated to be caused by the collection or infusion of cellular therapy product or by the product itself.
3. *Allogeneic* – refers to cells obtained from a donor and intended for infusion into a genetically distinct recipient.
4. *Autologous* – refers to cells obtained from a patient and intended for infusion into that patient.
5. *Applicant* – the natural or juridical person who is applying for Certificate of Accreditation (COA) of a health facility.
6. *Bioethics Advisory Board (BAB)* – the national body to examine the scientific, ethical, legal, and social issues arising from the biomedical research and development and recommends policies on stem cell and cell-based or cellular research and therapies in the Philippines.
7. *Bureau of Health Facilities and Services (BFS)* – the regulatory agency of DOH which shall exercise the accreditation function under these rules and regulations.
8. *Certificate of Accreditation (COA)* – a formal authorization issued by BHFSDOH to an individual, partnership, corporation or association to operate a facility that performs stem cell and cell-based or cellular transplantation. It refers to compliance with standards set for a particular purpose. These standards cover input/structural process and outcome/output standards.
9. *Cellular Theraphy* – the administration of products with the intent of providing effector cells in the treatment of disease or support of other therapy.
10. *Clinical Laboratory* – a facility where tests are done on specimens from the

human body to obtain information about the health status of patient for the prevention, diagnosis and treatment of diseases. The tests include, but are not limited to, the following disciplines: clinical chemistry, hematology, immunohematology, molecular biology and cytogenetics. The total testing process includes pre-analytical, analytical and post analytical procedures. Facilities that are involved in the pre-analytical processes such as collection, handling or preparation of specimens or act as mailing or distribution center such as in a laboratory network or system are also considered to be a part of a clinical laboratory. Refer to Administrative Order (A.O.) No. 2007-0027 entitled "Rules and Regulations Governing the Licensure and Regulation of Clinical Laboratories in the Philippines".

11. *Clinical Program* – an integrated medical team housed in geographically contiguous or proximate space with a single Clinical Program Director and common staff training programs , protocols, and quality management systems.

12. *Communicable Diseases* – refers to, but are not limited to, those transmitted by viruses, bacteria, fungi, parasites, and transmissible spongiform encephalopathy agents.

13. *Current Good Tissue Practice (cGTP)* - refers to requirements that govern the methods used, in, and the facilities and controls used for , the manufacture of human cells, tissues, and cellular and tissue-based products (HCT/Ps) in a way that prevents the introduction, transmission, or spread of communicable diseases by HCT/Ps.

14. *Current Good Manufacturing Practice (cGMP)* – the set of current practices followed by entities producing drug and biologic products, including cellular therapy products, to ensure that the products produced meet specific requirements for identity, strength, quality, and purity.

15. *Department of Health (DOH)*

16. *Donor* – a person who is the source of cells or tissue for a cellular therapy product.

17. *Expansion* - refers to growth of one or more cell populations in an in vitro culture system.

18. *Facility* – a location where activities covered by these Standards are performed. Such activities include determination of donor eligibility suitability, product collection, processing, storage, distribution, issue and administration. (As guidance, refer to FACT-JACIE International Standards for Cellular Therapy 5th Edition 2012). A facility, under this Order, may be any or all of the following:

a. Collection Facility - an entity providing the service of cellular therapy product collection.
b. Processing Facility – a location where cellular therapy product processing activities are performed in support of Clinical Program.
c. Storage Area/Facility – an entity holding a cellular therapy product or future processing, distribution or administration.

19. *Foundation for the Accreditation of Cellular Therapy (FACT)* and the Joint Accreditation Committee – International Society for Cellular Therapy [ISCT] and European Group for Blood and Marrow Transplantation [EBMT] (JACIE) – refers to the current Standards designed to promote quality medical and laboratory practice in hematopoietic progenitor cell transplantation and other therapies using cellular products.

20. *Genetic Manipulation* – refers to an ex vivo procedure(s) that genetically alters cell populations. A significant stem cell manipulation involves any process that alters the biological and/or physiological characteristics of cells or tissues including

introduction of viral genes and other genetic processes that incorporate exogenous genetic material into the genome of the recipient cells.
21. *Good Manufacturing Practice (GMP)* – refers to that part of quality assurance which ensures that medicinal products are consistently produced and controlled in accordance with quality standards appropriate for their intended use and as required by the applicable marketing authorization or product specifications.
22. *Human Tissue* – refers to cells obtained from any living or cadaveric human donor or organ.
23. *Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)* – articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion or transfer into a human recipient.
24. *Institutional Review Committee (IRC) or Ethics Committee or Ethical Review Committee (ERC)* – a Committee established by an institution in accordance with the regulations of the relevant governmental agency to review biomedical and behavioral research that involves human subjects and is conducted at or supported by that institution.
25. Pharmaceutical Inspection Cooperation Scheme (PIC/S) – refer to A.O. No. 2012-0008 entitled "Adoption and Implementation of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) Guides for the Good Manufacturing Practice (GMP) for Medical Products', Parts I and II and its Annexes. 26. *Philippine Food and Drug Administration (Phil. FDA)* – the agency of DOH in the Philippines charged with the regulation of stem cell and cell- based or cellular products.
27. *Prohibited* – refers to procedures, preparations or products that shall not be allowed or permitted for development or commercial use without exemption. These are banned or forbidden by law.
28. *Protocol* – a written document describing steps of a treatment or procedure in sufficient detail such that the treatment or procedure can be reproduced repeatedly without variation.
29. *Quality Assurance Program (QAP)* – an organized plan of activities that aims to provide the best possible care and services for all patients.
30. *Restricted* – refers to procedures, preparations or products that shall not be allowed unless a prior regulatory approval is obtained. These are controlled by law or rules and limited to authorized activities. These are stem cell products that have genetic manipulation.
31. *Registered and Permitted* – refers to procedures, preparations and products allowed to be in trade by the Phil. FDA, and in facilities with prior DOH accreditation. These are certified officially and legally by the government office for specific activities. These are stem cell products that do not have genetic manipulation.
32. *Standard Operating Procedures (SOP)/ Operational Manual* – refers to a compilation of written policies and detailed instructions required to perform the defined activities of the accredited facilities.
33. *Stem Cell* – undifferentiated cells from multicellular organism that have the capacity to divide and differentiate into different types of cells found in the body.
34. *Stem Cell-Based Products* - comprised of human cells, tissues, and cellular and tissues-based products (HCT/Ps) that are subject to Phil. FDA regulations.

V. IMPLEMENTING MECHANISMS

A. GENERAL GUIDELINES

1. Human stem cell and cell-based or cellular therapies shall be performed only in health facilities accredited by DOH.
2. Physicians shall ensure that patients are well-informed on stem cell and cell-

based/ cellular therapies and shall empower their patients with knowledge about treatment options that are available.
3. Each health facility shall have an IRC that shall review and evaluate the policies and procedures of stem cell and cell-based/cellular research and therapy in accordance with acceptable standards of practice. DOH standards and international guidelines.
4. Investigators/researchers shall obtain specific approvals from institutional committees and designated central authorities for the protocols that they plan to follow in their studies. Each facility and individual should analyze their practices and procedures to determine whether additional standards may apply.
5. Non hospital based facilities engaging in human stem cell and cell-based or cellular therapies in the Philippines shall have linkage with at least one (1) Level three (3) hospital licensed by DOH through a contractual agreement.
6. A system shall be established and maintained to implement, follow, review, and as needed, revise on an ongoing basis the regulatory framework for stem cell and cell-based or cellular research and therapy in the Philippines.
7. Stakeholders shall comply with the standards and requirements prescribed by BHFS and Phils. FDA in the assessment tool for accreditation of facilities utilizing human stem cell and cell-based or cellular therapies. The regulatory agencies took into consideration PIC/S guide for GMP, and appropriate cGMP, cGTP, current edition of FACT, this Order, and other policy guidelines.

B. SPECIFIC GUIDELINES

These specific guidelines under the Phil. DOH and Phil. FDA shall supersede any other policies and guidelines on cellular therapies, such as those issued by other countries and international bodies.

1. STEM CELL PREPARATIONS AND THERAPIES

a. PROHIBITED

The following stem cell preparations and therapies shall be prohibited from creation, importation, promotion, marketing and use.

1. Creation of human embryos for research purposes;
2. Human embryonic stem cells and their derivatives for human treatment and research;
3. Aborted human fetal stem cells and their derivatives for human treatment and research;
4. Plant parts labeled as stem cells.

b. RESTRICTED

The following stem cell preparations and therapies shall not be allowed for importation, promotion, marketing and use in humans without prior regulatory application and approval from Phil. FDA.

1. Genetically altered human adult stem cells for human treatment;
2. Genetically altered human umbilical cord stem cells for human treatment;
3. Adipose (Fat) derived human stem cell;
4. Any human cells, tissues, and cellular and tissue-based product (HCT/Ps) that are subjected to genetic manipulation, as defined in Section IV of this Order;