

HOUSE OF REPRESENTATIVES STAFF ANALYSIS

BILL #: HB 1185 Use of Stem Cells in a Clinic Setting
SPONSOR(S): Brodeur
TIED BILLS: **IDEN./SIM. BILLS:** SB 1508

REFERENCE	ACTION	ANALYST	STAFF DIRECTOR or BUDGET/POLICY CHIEF
1) Health Quality Subcommittee	12 Y, 0 N	Siples	McElroy
2) Appropriations Committee			
3) Health & Human Services Committee			

SUMMARY ANALYSIS

A stem cell is a cell that has the ability to develop into a specialized cell in the body. Stem cell therapy, also called regenerative medicine, is the use of stem cells to treat or prevent a disease or condition. The use of stem cells have shown potential in regenerative and reconstructive medicine and most recently those stem cells that are derived from adipose tissue have been marketed to treat a range of conditions, from macular degeneration to Parkinson's disease. These practices are regulated by the United States Food and Drug Administration (FDA); however, there has been some confusion amongst providers as to the applicability of FDA regulations to the practice. In November 2017, the FDA issued guidelines clarifying that adipose tissue-derived stem cells were subject to FDA regulations.

HB 1185 authorizes the Department of Health (DOH) to regulate clinics that use or purport to use stem cells in the treatment of its patients. The bill require each stem cell clinic to annually register with DOH and undergo inspections. A clinic does not have to register with DOH if it:

- Is licensed under ch. 395, F.S.;
- Is wholly owned and operated by one or more Florida-licensed physicians;
- Is affiliated with an accredited medical school that provides training to medical students, residents, or fellows; or
- Solely performs one or more of the following:
 - Collection of umbilical cord blood cells for blood banking;
 - Collection, transfer, or insemination of oocytes; or
 - Injection or infusion of platelet-rich plasma.

The bill requires that each clinic designate a physician who holds an active and unencumbered license to practice to be responsible for compliance with clinic registration and operation requirements.

The bill authorizes DOH to impose a fine or pursue administrative action if a clinic fails to comply with the registration requirement, DOH rules, the Florida Drug and Cosmetic Act, or the Federal Food, Drug, and Cosmetic Act and rules adopted thereunder.

The bill requires a physician who performs a procedure using or purporting to use stem cells or products containing stem cells to follow the applicable good manufacturing practices for collecting, removing, processing, implanting, and transferring stem cells or products containing stems cells, pursuant to the federal Food, Drug, and Cosmetic Act and federal law governing human cells, tissues, and cellular and tissue-based products. A physician who practices at an unregistered clinic may be disciplined by the appropriate regulatory board.

The bill will have an insignificant, recurring positive fiscal impact on DOH, and an insignificant negative fiscal impact on DOH, which current resources are sufficient to absorb. The bill has no fiscal impact on local governments.

The bill has an effective date of July 1, 2018.

FULL ANALYSIS

I. SUBSTANTIVE ANALYSIS

A. EFFECT OF PROPOSED CHANGES:

Present Situation

Stem Cells

Stem cells are cells that have the ability to divide for indefinite periods in culture and to give rise to specialized cells.¹ Under certain physiologic or experimental conditions, stem cells can be induced to become tissue- or organ-specific cells with special functions.² Stem cells are referred to as “undifferentiated” because they have not yet committed to a developmental path that will for a specific tissue or organ.³ Differentiation is the process of changing into a specific type of cell.⁴ Stem cells have the potential to repair, restore, replace, and regenerate cells, and could possibly be used to treat a number of medical conditions.⁵

Scientists primarily work with two categories of stem cells: embryonic and adult.⁶ Embryonic stem cells are derived from embryos, usually created by in vitro fertilization and donated for research with the informed consent of donors.⁷ Embryonic stem cells may be used to generate every cell type found in the body because they are pluripotent.⁸

Adult stem cells are more specialized than embryonic stem cells and typically generate different cell types for the specific tissue or organ in which they live.⁹ Adult stem cells have been found in organs that need to continuously replenish themselves, such as the blood, skin, and gut, but also are in other less generative organs such as the brain.¹⁰

In 2007, scientists identified conditions that would allow some specialized adult stem cells to be genetically reprogrammed or engineered to become pluripotent, i.e. behave like embryonic cells.¹¹ These reprogrammed cells are called induced pluripotent stem cells. It is not known if the induced pluripotent stem cells differ from embryonic stem cells in a clinically significant way.¹² However, induced pluripotent stem cells could replace the use of embryonic stem cells in research and clinics.¹³

Stem cell therapy is the treatment of a condition or illness with stem cells or cells that come from stem cells to replace or repair a patient’s damaged cells or tissues.¹⁴ Currently, the range of diseases for

¹ National Institutes of Health, *Stem Cell Information: Glossary*, available at <https://stemcells.nih.gov/glossary.htm> (last visited January 8, 2018).

² National Institutes of Health, *Stem Cell Information: Stem Cell Basics I.*, available at <https://stemcells.nih.gov/info/basics/1.htm> (last visited January 8, 2018).

³ National Institutes of Health, *Stem Cell Information: Stem Cell Basics II.*, available at <https://stemcells.nih.gov/info/basics/2.htm> (last visited January 8, 2018).

⁴ Id.

⁵ U.S. Food and Drug Administration, *FDA Warns about Stem Cell Therapies*, (Nov. 16, 2017), available at <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm286155.htm> (last visited January 8, 2018).

⁶ *Supra* note 2.

⁷ National Institutes of Health, *Stem Cell Information: Stem Cell Basics III.*, available at <https://stemcells.nih.gov/info/basics/3.htm> (last visited January 8, 2018).

⁸ Id. Pluripotent is the state of a single cell that is capable of differentiating into all tissues of an organism, but not alone capable of sustaining full organismal development (*supra* note 1).

⁹ International Society for Stem Cell Research, *Stem Cell Facts*, available at <http://www.closerlookatstemcells.org/docs/default-source/patient-resources/stem-cell-facts.pdf?sfvrsn=4> (last visited January 8, 2018).

¹⁰ Id.

¹¹ *Supra* note 9.

¹² National Institutes of Health, *Stem Cell Information: Stem Cell Basics VI.*, available at <https://stemcells.nih.gov/info/basics/6.htm> (last visited January 9, 2018).

¹³ Vimal Singh, et al, *Induced Pluripotent Stem Cells: Applications in Regenerative Medicine, Disease Modeling, and Drug Discovery*,

¹⁴ *Supra* note 9.

which there are proven treatments based on stem cell therapy is small.¹⁵ However, treatments for disorders of the blood and immune systems and acquired loss of bone marrow, can in some cases be treated effectively with blood stem cells.¹⁶ Tissue- and organ-specific treatments, such as those for skin and corneas, have proven successful.¹⁷ However, other stem cell therapies are experimental, and may not yet been shown to be safe or effective.¹⁸

In recent years, some practitioners have begun using adipose tissue packaged as a product called stromal vascular fraction (SVF), which are essentially adipose-derived stem cells.¹⁹ These adipose-derived stem cells have shown potential in regenerative and reconstructive medicine.²⁰ The use of adipose-derived stem cell-based therapies has been mostly harmless and sometimes beneficial.²¹ However, some treatments have caused vision loss, tumors, and death.²²

Stem Cell Regulation

The Center for Biologics Evaluation and Research (CBER), within the United States Food and Drug Administration (FDA), regulates biological products for human use, including gene therapy.²³ An establishment that manufactures human cells, tissues, and cellular and tissue-based products (HCT/Ps), must register with CBER, if the:²⁴

- The HCT/P is minimally manipulated;
- The HCT/P is intended for homologous use only;
- The manufacture of the HCT/P does not involve the combination of cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT; and
- Either:
 - The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
 - The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and:
 - Is for autologous use;
 - Is for allogeneic use in a first-degree or second-degree blood relative; or
 - Is for reproductive use.

An establishment is not required to comply with registration and reporting requirements if the establishment:²⁵

- Uses HCT/P's solely for nonclinical scientific or educational purposes;
- Removes HCT/P's from an individual and implants such HCT/P's into the same individual during the same surgical procedure;

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¹⁶ Id.

¹⁷ Id.

¹⁸ Id.

¹⁹ Hermes Taylor-Weiner, Ph.D., and Joshua Graff Zivin, Ph.D., *Medicine's Wild West – Unlicensed Stem-Cell Clinics in the United States*, N. ENGL. J. MED. 2015; 373:985-987, (Sept. 10, 2015), available at <http://www.nejm.org/doi/full/10.1056/NEJMp1504560?rss=mostEmailed> (last visited January 25, 2018).

²⁰ Pablo Bora and Anish S. Majumdar, *Adipose Tissue-Derived Stromal Vascular Fraction in Regenerative Medicine: A Brief Review of Biology and Translation*, *Stem Cell Research & Therapy* 8:145, (2017), available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5472998/pdf/13287_2017_Article_598.pdf (last visited January 25, 2018).

²¹ Id.

²² Id.

²³ U.S. Food and Drug Administration, *About the Center for Biologics Evaluation and Research*, available at <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/default.htm> (last visited January 25, 2018).

²⁴ 21 C.F.R. s. 1271.10.

²⁵ 21 C.F.R. s. 1271.15.

- Is a carrier who accepts, receives, carries, or delivers HCT/P's in the usual course of business as a carrier;
- Does not recover, screen, test, process, label, package, or distribute, but only receives or stores HCT/P's solely for implantation, transplantation, infusion, or transfer within your facility;
- Only recovers reproductive cells or tissue and immediately transfers them into a sexually intimate partner of the cell or tissue donor; or
- Is an individual under contract, agreement, or other arrangement with a registered establishment and engaged solely in recovering cells or tissues and sending the recovered cells or tissues to the registered establishment; however, it must comply with all other applicable requirements.

The HCT/P is regulated as a drug, device, or biologic product under the Public Health Service Act and/or the Food, Drug, and Cosmetics Act, if it does not meet the above-referenced requirements or qualify for an exemption.²⁶

In November 2017, the FDA issued guidance intended to improve stakeholders' understanding of the definitions of minimal manipulation and homologous use as used in its registration rule.²⁷ In its guidelines, the FDA states that adipose tissue is considered structural tissue.²⁸

Structural tissue is minimally manipulated if the processing of the tissue alters an original relevant characteristic of the tissue, relating to the tissue's utility for reconstruction, repair, or replacement as structural tissue.²⁹ The effects of the processing on the properties that contribute to the specific tissue's function in the donor must be considered determines whether the processing alters the original relevant characteristic of the tissue.³⁰ For example, the definition of minimal manipulation applies if the original relevant characteristic of adipose tissue relates to its utility to provide cushioning and support, but the manufacturer recovers adipose tissue by liposuction and processes the adipose tissue to isolate cellular components (SVF).³¹ In this example, the HCT/P is considered more than minimally manipulated because the processing breaks down and eliminates the adipocytes and structural components that provide cushioning and support.³² Therefore, the HCT/P would be regulated as a biologic product, and would require a premarket review, such as clinical trials prior to widespread use of the product.³³ Under the Food, Drug, and Cosmetic Act, the manufacturer must obtain a license from the FDA to lawfully market the biologic product.³⁴

In November 2017, the FDA announced plans to increase its regulation of clinics who use therapies involving biologic products that have not been approved by the FDA.³⁵ The only stem cell-based therapies that have been approved by the FDA for use in the United States consist of blood-forming stem cells derived from cord blood.³⁶

Regulation of Physicians in Florida

²⁶ 21 C.F.R. s. 1270.20.

²⁷ CBER, *Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use: Guidance for Industry and Food and Drug Administration Staff*, (Nov. 2017, corrected Dec. 2017), available at <https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/UCM585403.pdf> (last visited January 26, 2018).

²⁸ *Id.* at 8.

²⁹ *Id.*

³⁰ *Id.* at 11.

³¹ *Id.* at 13.

³² *Id.*

³³ FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D., on the FDA's New Policy Steps and Enforcement Efforts to Ensure Proper Oversight of Stem Cell Therapies and Regenerative Medicine*, (Aug. 28, 2017), available at <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573443.htm> (last visited January 26, 2018).

³⁴ 42 U.S.C. s. 262.

³⁵ *Supra* note 33.

³⁶ *Supra* note 5.

The Board of Medicine and the Board of Osteopathic Medicine (collectively, Boards), within the Department of Health (DOH), have authority to adopt rules to regulate practice of medicine and osteopathic medicine, respectively. The Boards have authority to establish, by rule, standards of practice and standards of care for particular settings.³⁷ Such standards may include education and training, medications including anesthetics, assistance of and delegation to other personnel, sterilization, performance of complex or multiple procedures, records, informed consent, and policy and procedures manuals.³⁸

In 2015, the Florida Board of Medicine warned physicians and consumers that they should be aware of the risks involved accessing stem cell therapies and regenerative medicine that has not approved by the FDA.³⁹ The Board of Medicine further warned that a physician providing stem cell treatment should have investigational new drug application (IND) or a single patient IND for Compassionate or Emergency Use.⁴⁰ Florida does not specifically regulate clinics who perform treatments using stem cells; however, the Board of Medicine and the Board of Osteopathic Medicine, have authority to investigate and discipline physicians who fail to meet the standard of care for providing medical services. In 2013, the Board of Medicine revoked the licenses of two physicians in administrative cases involving stem cells for failing to meet the standard of care.⁴¹

Effect of Proposed Changes

Clinic Registration

HB 1185 requires a clinic⁴² or physician who advertises, uses, or purports to use stem cells or products containing stems cells to register with DOH. The bill refers only to a stem cell that is an allogenic or autologous cell that is altered to become undifferentiated, losing its original structural function, so that it can become a specialized cell type.⁴³ A clinic does not have to register with DOH if it:

- Is licensed under ch. 395, F.S.;⁴⁴
- Is wholly owned and operated by one or more Florida-licensed physicians;
- Is affiliated with an accredited medical school that provides training to medical students, residents, or fellows; or
- Solely performs one or more of the following:
 - Collection of umbilical cord blood cells for blood banking;
 - Collection, transfer, or insemination of oocytes; or
 - Injection or infusion of platelet-rich plasma.

A clinic must register each of its locations separately. A clinic or physician must submit a new registration if there is a change of ownership. DOH may fine the clinic or physician, as well as the new owner up to \$5,000 per day for each location.

The bill requires each clinic must designate a physician who holds an active and unencumbered license to practice to be responsible for compliance with clinic registration and operation requirements. A clinic

³⁷ Sections 458.331(v) and 459.015(z), F.S.

³⁸ Id.

³⁹ Florida Board of Medicine, *Information on Stem Cell Clinics Offering Unapproved Therapies*, available at <http://flboardofmedicine.gov/latest-news/october-2015-newsletter/>.

⁴⁰ Id.

⁴¹ Department of Health, *2018 Agency Analysis for House Bill 1185*, (Jan. 12, 2018), on file with the Health Quality Subcommittee.

⁴² The bill defines a clinic as a privately or publicly owned facility or office that advertises a service that uses or purports to use stem cells or a product containing stem cells to diagnose, cure, mitigate, treat, provide therapy for, or prevent an injury or disease; or performs any procedure that is intended to diagnose, cure, mitigate, treat, provide therapy for, or prevent an injury or disease that uses or purports to use stem cells or a product containing stem cells which has not been approved by or is not the subject of a clinical trial approved by the U.S. Food and Drug Administration

⁴³ The bill specifically excludes stem cells that are only rinsed, cleaned, or sized and remain differentiated.

⁴⁴ Chapter 395, F.S., governs the licensure and regulation of hospitals.

must notify DOH within 10 days of a change in the designated physician. If a clinic fails to have a designated physician, DOH may issue an emergency suspension⁴⁵ of the clinic's registration.

The bill authorizes DOH to impose a fine of up to \$5,000 per violation if a clinic fails to comply with the registration requirement, DOH rules, the Florida Drug and Cosmetic⁴⁶ Act, or the Federal Food, Drug, and Cosmetic Act and rules adopted thereunder. When determining if a fine should be imposed and the amount of the fine, DOH must consider:

- The gravity of the violation, including the existence and severity of patient deception, serious or physical mental harm, or the potential of such deception or harm;
- The actions taken by the physician, clinic, or designated physician to correct the violation;
- Whether there were previous violations at the clinic; and
- The financial benefits derived by the physician, clinic, or designated physician from committing or continuing to commit the violation.

If the physician, clinic, or designated physician fails to cease the violating behavior as of the date required by DOH, each day the violation continues constitutes an additional, separate, and distinct violation. DOH may impose a fine if the designated physician knowingly misrepresents that action had been taken to correct a violation. However, if it is an owner-operated clinic, DOH may impose a fine and revoke or deny a clinic registration.

The bill requires DOH to adopt rules for the implementation of the registration requirement, as well as an annual inspection of registered clinics. All costs for the registration and inspections must be borne by the clinic. The board must also adopt rules addressing advertising, adverse incident reporting, and informed consent.

Physician Responsibilities

The bill requires a physician who performs a procedure using or purporting to use stem cells or products containing stem cells must follow the applicable good manufacturing practices for collecting, removing, processing, implanting, and transferring stem cells or products containing stems cells, pursuant to the federal Food, Drug, and Cosmetic Act⁴⁷ and federal law governing human cells, tissues, and cellular and tissue-based products.⁴⁸

A physician who practices at a clinic that is not registered as required may be disciplined by the appropriate regulatory board.

The bill provides an effective date of July 1, 2018.

B. SECTION DIRECTORY:

Section 1: Creates s. 458.352, F.S., relating to use of stem cells in a clinic setting.

Section 2: Creates s. 459.207, F.S., relating to use of stem cells in a clinic setting.

Section 3: Provides an effective date of July 1, 2018.

II. FISCAL ANALYSIS & ECONOMIC IMPACT STATEMENT

A. FISCAL IMPACT ON STATE GOVERNMENT:

⁴⁵ DOH may issue an emergency suspension, restriction, or limitation of a license if it finds that an immediate serious danger to the public health, safety, welfare exists.

⁴⁶ Chapter 499, F.S.

⁴⁷ 21 U.S.C. ss. 301, et seq., and 52 Stat. 1040 et seq.

⁴⁸ 21 C.F.R. s. 1271.

1. Revenues:

The bill will have an insignificant, recurring positive fiscal impact from the fees collected for the registration and inspection of stem cell clinics.⁴⁹ DOH estimates 20 clinics will register.

2. Expenditures:

The bill will have an insignificant, recurring negative fiscal impact due to an increase in workload associated with the registration, inspection, and regulation of clinics that use stem cells, which current resources are adequate to absorb.⁵⁰

The bill will have an insignificant, nonrecurring negative fiscal impact for costs related to rulemaking and to update the Licensing and Enforcement Information Database System (LEIDS), which current resources are adequate to absorb.⁵¹

B. FISCAL IMPACT ON LOCAL GOVERNMENTS:

1. Revenues:

None.

2. Expenditures:

None.

C. DIRECT ECONOMIC IMPACT ON PRIVATE SECTOR:

Clinics using stem cells will be required to pay registration and inspection fees.

D. FISCAL COMMENTS:

None.

III. COMMENTS

A. CONSTITUTIONAL ISSUES:

1. Applicability of Municipality/County Mandates Provision:

Not Applicable. This bill does not appear to affect county or municipal governments.

2. Other:

None.

B. RULE-MAKING AUTHORITY:

The bill provides DOH sufficient rulemaking authority.

C. DRAFTING ISSUES OR OTHER COMMENTS:

None.

⁴⁹ *Supra* note 41.

⁵⁰ *Id.*

⁵¹ *Id.*

IV. AMENDMENTS/ COMMITTEE SUBSTITUTE CHANGES