The Florida Senate

BILL ANALYSIS AND FISCAL IMPACT STATEMENT

(This document is based on the provisions contained in the legislation as of the latest date listed below.)

Prepared By: The Professional Staff of the Committee on Health Policy

BILL:	SB 512
INTRODUCER:	Senator Hutson
SUBJECT:	Nonembryonic Stem Cells
DATE:	February 3, 2020
REVISED:	

	ANALYST	STAFF DIRECTOR	REFERENCE	ACTION
1.	Rossitto-Van Winkle	Brown	HP	**Pre-meeting**
2.			AP	
3.			RC	

I. Summary:

SB 512 creates s. 381.4017, F.S., which authorizes stem cell banks to operate in Florida. The bill requires stem cell banks to register with the Department of Health (DOH), and supply certain information. The bill authorizes:

- The self-administration of non-embryonic stem cells;
- The administration of non-embryonic stem cells by persons licensed or authorized to administer, or assist in the administration of, medications or health care;
- A pharmacy, owned or operated in Florida, or both, to compound health care products using nonembryonic stem cells either alone or with other sterile ingredients
- A person to import any sterile compound, drug, or other treatment containing nonembryonic stem cells if such compound, drug, or other treatment:
  - Was obtained legally from the jurisdiction from which it came; and
  - Is for personal use.

The bill requires:

- A stem cell bank to register with the DOH before it organizes or begins operation and to provide specific information on a DOH-approved form;
- A stem cell bank to carry liability insurance in an unspecified limits; and
- The DOH to make rules that adopt standards developed by an independent third party as that term is defined in the bill.

The bill provides an effective date of July 1, 2020.

II. Present Situation:

Stem Cells

Stem cells are unspecialized cells that have the ability to divide for indefinite periods of time in culture medium and to give rise to specialized cells.[1] Stem cells have the potential to develop into many different types of cells during early life and growth. In addition, in many human tissues, stem cells serve as an internal repair system, dividing essentially without limit, to replenish other cells as long as a person is still alive. When a stem cell divides, each new cell has the potential to either remain an undifferentiated stem cell or become a cell with a specialized function such as a muscle, red blood, or brain cell.[2]

Stem cells are distinguished from other cells by two important characteristics:
- Unspecialized cells capable of renewing themselves through cell division; and
- The ability to be induced to become tissue-specific or organ-specific cells under certain physiologic or experimental conditions.[3]

In some organs – such as the alimentary canal (gut) – and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, such as the pancreas and the heart, stem cells only divide under special conditions.[4]

Until recently, scientists primarily worked with two kinds of stem cells from animals and humans:
- Embryonic stem cells;[5] and
- Non-embryonic "somatic," or "adult," stem cells.[6]

Stem cells offer new potentials for treating diseases such as diabetes and heart disease, given their unique regenerative abilities. More research is needed to understand how to use these cells for cell-based therapies to treat disease. This practice is referred to as regenerative or reparative medicine.[7]

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[1] National Institutes of Health, Stem Cell Information, Glossary, *Stem Cells* https://stemcells.nih.gov/glossary.htm#stemcells (last visited Jan. 27, 2020).
[2] National Institutes of Health, Stem Cell Information, *Stem Cell Basics I.*, https://stemcells.nih.gov/info/basics/1.htm (last visited Jan. 27, 2020).
[3] *Id.*
[4] *Id.*
[5] Embryonic stem cells are primitive undifferentiated cells that are derived from preimplantation-stage embryos. They are capable of dividing without differentiating for a prolonged period in culture; and are known to develop into cells and tissues of the three primary germ layers. The three germ layers are the ectoderm, the mesoderm, and the endoderm. *See* National Institutes of Health, Stem Cell Information, Glossary, *Embryonic Stem Cells,* https://stemcells.nih.gov/glossary.htm#stemcells (last visited Jan. 27, 2020).
[6] Somatic (adult) stem cells are relatively rare undifferentiated cells found in many organs and differentiated tissues with a limited capacity for both self-renewal (in the laboratory) and differentiation. Such cells vary in their differentiation capacity, but it is usually limited to cell types in the organ of origin. *See* National Institutes of Health, Stem Cell Information, Glossary, *Somatic (adult) Stem Cells,* https://stemcells.nih.gov/glossary.htm#stemcells (last visited Jan. 27, 2020).
[7] National Institutes of Health, *Stem Cell Basics I.*, https://stemcells.nih.gov/info/basics/1.htm (last visited Jan. 27, 2020).

Federal Regulation of Stem Cells

Under 21 C.F.R. 1271, certain stem cells are labeled as a drug[8] and subject to FDA regulation if the stem cell has been derived from structural tissue or non-structural tissue in a manufacturing process involving more than minimal manipulation.[9]

The FDA regulates articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion or transfer into a human recipient as human cells, tissues, or cellular or tissue-based products (HCT/Ps) which are known as stem cells.[10]

The U.S. Center for Biologics Evaluation and Research (CBER) regulates HCT/Ps.[11] The CBER does not regulate the transplantation of vascularized human organ transplants such as the kidney, liver, heart, lung, or pancreas. The Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services oversees the transplantation of vascularized human organs.[12]

Minimally manipulated bone marrow is also used in stem cell treatments but is not considered by the FDA to be an HCT/Ps,[13] and thus is not regulated by the FDA.[14] The HRSA regulates minimally manipulated bone marrow stem cells used for transplant.[15]

Due to the unique nature of HCT/Ps, the FDA uses a tiered, risk-based approach to the regulation of HCT/Ps, rather than the Federal Food, Drug and Cosmetic Act (FDCA), for products that meet the definition of a drug, biologic, or device.[16] The tiered, risk-based approach includes

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[8] See 21 U.S.C. s. 321(g). The FDA defines a "drug" as an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and "articles (other than food) intended to affect the structure or function of the body."

[9] U.S Department of Health and Human Services, Food and Drug Administration, Center for Evaluation and Research, Center for Devices and Radiological Health, Office of Combination Products, (Nov. 2017, corrected Dec. 2017), *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,* (December 2017) *available at* https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/cellularandgenetherapy/ucm585403.pdf (last visited Jan. 27, 2020). Section 1271.10(a)(1) provides that one of the criteria for an HCT/P to be regulated solely under s. 361 of the PHSA and the regulations in Part 1271, is that the HCT/P is only "minimally manipulated." As defined in 21 CFR 1271.3(f), "minimal manipulation" means: 1) For *structural tissue*, processing that *does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement* (emphasis added); or 2) For *cells or nonstructural tissues*, processing *does not alter the relevant biological characteristics of cells or tissues*. Note: the FDA considers the processing of an HCT/P to be, "more than minimal manipulation," if information does not exist to show that the HCT/P qualifies for regulation solely under s. 361 of the PHSA. *See* 21 C.F.R. 1271.21 and 1271.10.

[10] 21 C.F.R. 1271.3(d).

[11] See 21 C.F.R., 1270 and 1271. The CBER is a part of the Food and Drug Administration.

[12] U.S. Food and Drug Administration, *Tissue and Tissue Products* (as of July 11, 2019), *available at* https://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/default.htm (last visited Jan. 27, 2020).

[13] *See* 21 C.F.R. 1271.3(d)(4).

[14] U.S. Food and Drug Administration, Food and Drug Administration, *FDA Warms About Stem Cell Therapies*, https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm286155.htm (last visited Jan. 27, 2020).

[15] U.S. Department of health and Human Services, Health Resources and Services Administration, *Healthcare Systems, available at* https://www.hrsa.gov/sites/default/files/ourstories/organdonation/factsheet.pdf (last visited Jan. 27, 2020).

[16] Although the FDA is authorized to apply the requirements in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act to those products that meet the definition of drug, biologic, or device, under this tiered, risk-based approach, those HCT/Ps that meet specific criteria or fall within detailed exceptions do not require premarket review or approval. *See* U.S Department of Health and Human Services, Food and Drug Administration, Center for Evaluation and

recommendations on how the transmission of communicable diseases can be prevented; the process controls necessary to prevent contamination and preserve the integrity and function of the products; and how clinical safety and effectiveness can be assured.[17]

The tiered, risk-based approach is contained in regulations referred to as the "tissue rules" issued by the FDA under the communicable disease authority of s. 361 of the Public Health Service Act (PHSA).[18]

For an HCT/P to be regulated solely under the requirements of s. 361 of the PHSA and 21 C.F.R. 1271, it must meet all of the following criteria:[19]

- The HCT/P is minimally manipulated;[20]
- The HCT/P is intended for homologous use only;[21]
- The HCT/P is not combined with any other article, except water, crystalloids, or a sterilizing, preserving, or storage agent; and
- The HCT/P either:
  - Does not have a systemic effect and is not dependent upon the metabolic activity of living cells, for its primary function; or
  - Has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and is for:
    - Autologous use;[22]
    - Allogeneic use;[23] or
    - Reproductive use.[24]

Research, Center for Devices and Radiological Health, Office of Combination Products, Nov. 2017, corrected Dec. 2017, *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*, https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/cellularandgenetherapy/ucm585403.pdf (last visited Jan. 27, 2020).

[17] *Id.*

[18] 42 U.S.C. s. 264.

[19] 21 C.F.R. 1271.10.

[20] 21 C.F.R. 1271.10(a)(1) provides that one of the criteria for an HCT/P to be regulated solely under s. 361 of the PHSA and the regulations in 1271, is that the HCT/P is only "minimally manipulated". As defined in 21 C.F.R. 1271.3(f), "minimal manipulation" means: 1) For *structural tissue*, processing that *does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement* (emphasis added); or 2) For *cells or nonstructural tissues*, processing *does not alter the relevant biological characteristics of cells or tissues*. Note: the FDA considers the processing of an HCT/P to be, "more than minimal manipulation," if information does not exist to show that the HCT/P qualifies for regulation solely under s. 361 of the PHSA.

[21] 21 C.F.R. 1271.10(a)(2), provides that one of the criteria for an HCT/P to be regulated solely under s. 361 of the PHSA, and the regulations in 1271, is that the "HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent." As defined in 21 C.F.R. 1271.3(c), "homologous use" means the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor. This criterion reflects the FDA's conclusion that there would be increased safety and effectiveness concerns for HCT/Ps that are intended for a non-homologous use, because there is less basis on which to predict the product's behavior. *See supra* note 8, at 4.

[22] *"Autologous use"* means the implantation, transplantation, infusion, or transfer of human cells or tissue back into the individual from whom the cells or tissue were recovered. *See* 21 C.F.R. 1271.3(a).

[23] *"Allogeneic use"* means taken from different individuals of the same species. Two or more individuals are said to be allogeneic to one another when the genes at one or more loci are not identical. Medicinenet.com, *Medical Definition of Allogeneic*, https://www.medicinenet.com/script/main/art.asp?articlekey=25266 (last visited Jan. 27, 2020).

[24] 21 C.F.R. 1271.10(a).

To apply the minimally manipulated criteria, the FDA first determines if the HCT/P to be transplanted was derived from structural tissue or cellular/nonstructural tissue. This determination is made based on the characteristics of the HCT/P in the donor, prior to recovery, and before any processing takes place.[25]

In applying the minimally manipulated analysis, the FDA acknowledges that HCT/Ps perform multiple functions and that structural tissues contain cells. The FDA also acknowledges that some manufacturers assert that an HCT/P has both a structural and cellular/nonstructural function. However, under FDA regulations, HCT/Ps are considered either structural tissues or cells/nonstructural tissues. HCT/Ps that physically support or serve as a barrier or conduit, or connect, cover, or cushion, are generally considered structural tissues for the purpose of applying the HCT/P regulatory framework. The FDA gives the following examples of what it considers structural tissue: bone, skin, amniotic membrane and umbilical cord, blood vessel, adipose tissue, articular cartilage, non-articular cartilage, and tendon or ligament.[26]

HCT/Ps that serve metabolic or other biochemical roles in the body, such as hematopoietic, immune, and endocrine functions, are generally considered cells/nonstructural tissues for the purpose of applying the FDA HCT/P regulatory framework. The FDA examples of cells or nonstructural tissues include: reproductive cells or tissues (oocytes), hematopoietic stem/progenitor cells (cord blood), lymph nodes and thymus, parathyroid glands, peripheral nerve, and pancreatic tissue.[27]

The FDA defines "processing" as any activity performed on an HCT/P, other than: rinsing, cleaning, recovery, donor screening, donor testing, storage, sizing, labeling, packaging, distribution, testing for microorganisms, preparation, sterilizations, steps to inactivate or remove adventitious agents, preservation for storage, and removal from storage.[28] Under this definition, processing includes: cutting, grinding, shaping, culturing, enzymatic digestion, and decellurization.[29]

An HCT/P is exempt from registration and regulation under the PHSA and 21 C.F.R. 1271, if the establishment:[30]

- Uses the HTC/Ps solely for nonclinical scientific or educational purposes;
- Removes HCT/Ps from an individual and implants such HCT/Ps into the same individual, during the same surgical procedure;
- Is a carrier who accepts, receives, carries, or delivers HCT/P's in the usual course of business;

[25] *Supra* note 9.
[26] *Id.*
[27] *Supra* note 9.
[28] See 21 C.F.R. 1271.3(ff).
[29] *Supra* note 9.
[30] Establishment means a place of business under one management, at one general physical location, that engages in the manufacture of human cells, tissues, and cellular and tissue-based products. Establishment includes: (1) Any individual, partnership, corporation, association, or other legal entity engaged in the manufacture of human cells, tissues, and cellular and tissue-based products; and (2) Facilities that engage in contract manufacturing services for a manufacturer of human cells, tissues, and cellular and tissue-based products. 21 C.F.R. 1271.3(b).

- 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 its facility; or
- Only recovers reproductive cells or tissue and immediately transfers them into a sexually intimate partner of the cell or tissue donor.

If an individual is under contract with a registered establishment, and engaged solely in recovering cells or tissues and sending the recovered cells or tissues to the registered establishment, he or she is not required to register or list the establishment's HCT/Ps independently, but he or she must comply with all other applicable requirements. [31]

If an HCT/P does not meet the above criteria, and the manufacturer of the HCT/P does not qualify for an exception,[32] the HCT/P will be regulated as a drug, device, and/or biological product under the FDCA, the PHSA,[33] and applicable regulations;[34] and premarket review will be required.[35]

According to the FDA, if a manufacturer or establishment isolates cells from structural tissue to produce a cellular therapy product, the definition of minimal manipulation applies regardless of the method used to isolate the cells. The definition applies because the assessment of whether the HCT/P is a structural tissue or cellular/nonstructural tissue is based on the characteristics of the HCT/P as it exists in the donor, prior to recovery, and prior to any processing that takes place.[36]

Federal law requires tissue establishments[37] that do not meet an exemption to:
- Screen and test donors;
- Prepare and follow written procedures for prevention of the spread of communicable disease; and
- Maintain records.[38]

The FDA has published rules to broaden the scope of products subject to regulation and to include more comprehensive requirements to prevent the introduction, transmission, and spread of communicable disease. Those rules include requiring tissue establishments to:
- Register and submit a list to the FDA of every HCT/P it manufactures within five days after operations begin, or within 30 days of the effective date of the registration;[39]
- Determine donor eligibility, including screening and testing;[40] and

[31] 21 C.F.R. 1271.15.
[32] 21 C.F.R., 1271.10, 1271.15 and 1271.155.
[33] 42 U.S.C. s. 262.
[34] 21 C.F.R. 1271.
[35] *Supra* note 9.
[36] *Id.*
[37] *Supra* note 31.
[38] *See* 21 C.F.R 1270 and 1271.2121.
[39] 21 C.F.R. 1271.21.
[40] 21 C.F.R. 1271.45.

- Recover, process, store, label, package, and distribute HCT/Ps, and screen and test cell and tissue donors, in such a way that prevents the introduction, transmission, or spread of communicable diseases.[41]

The requirements are intended to improve protection of the public health while minimizing regulatory burden.[42]

The only HCT/Ps that are FDA-approved for use in the United States consist of blood-forming stem cells, referred to as hematopoietic progenitor cells, derived from cord blood. These products are approved for limited use in patients with disorders that affect the hematopoietic system – the body system that is involved in the production of blood. The FDA-approved stem cell products are listed on the FDA website.[43]

Florida Regulation of Stem Cells

Stem Cell Preparation/Manufacturing

The registration of stem cell banks does not exist under current Florida law. The Department of Business and Professional Regulation (DBPR) administers and enforces the Florida Drug and Cosmetic Act (FDCA) to prevent fraud, adulteration, misbranding, or false advertising in the preparation, manufacture, repackaging, or distribution of drugs, devices, and cosmetics.[44] In Florida, "a person may not sell, offer for sale, hold for sale, manufacture, repackage, distribute, or give away any new drug unless an approved application has become effective under the federal act or unless otherwise permitted by the Secretary of the United States Department of Health and Human Services for shipment in interstate commerce."[45]

The FDCA defines a "drug" as an article, or a component of an article,[46] that is:

- Recognized in the current edition of the United States Pharmacopoeia and National Formulary (USP-FM),[47] official Homeopathic Pharmacopoeia of the United States (HPUS),[48] or any supplement to any of those publications;

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[41] *Id.*

[42] U.S. Department of Health and Human Services, Food and Drug Administration, *Tissue and Tissue Products*, https://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/default.htm (last visited Jan. 31, 2020).

[43] U.S. Department of Health and Human Services, Food and Drug Administration, *FDA Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P's) Product List* (page updated Feb. 2, 2018) *available at* https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/fda-regulation-human-cells-tissues-and-cellular-and-tissue-based-products-hctps-product-list (last visited Jan. 31, 2020).

[44] *See* part I of ch. 499, F.S.

[45] Section 499.023, F.S.

[46] Includes active pharmaceutical ingredients, but does not include devices or their non-drug components, parts, or accessories. *Also see* Section 499,003(1), F.S. The term "active pharmaceutical ingredient" includes any substance or mixture of substances intended, represented, or labeled for use in drug manufacturing that furnishes or is intended to furnish, in a finished dosage form, any pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, therapy, or prevention of disease in humans or other animals, or to affect the structure or any function of the body of humans or animals.

[47] USP-NF is a combination of two compendia, the United States Pharmacopeia (USP) and the National Formulary (NF). It contains standards for medicines, dosage forms, drug substances, excipients, biologics, compounded preparations, medical devices, dietary supplements, and other therapeutics. *See* 21 U.S.C. s. 301(g)(1).

[48] The HPUS is declared a legal source of information on drug products (along with the USP/NF) in the Federal Food Drug and Cosmetic Act, 21 U.S.C. § 301. Section 201(g)(1) of the Act. 21 U.S.C. s. 321 defines the term "drug" as articles

- Intended for use in the diagnosis, cure, mitigation, treatment, therapy, or prevention of disease in humans or other animals;
- Intended to affect the structure or any function of the body of humans or other animals; or
- Intended for use as a component of any article:
  - Listed in the USP-FM, or HPUS;
  - Used in the diagnosis, cure, mitigation, treatment, therapy, or prevention of disease in humans or other animals;
  - Used to affect the structure or any function of the body of humans or other animals; and
  - That includes active pharmaceutical ingredients.[49]

The FDCA defines the manufacturing of a drug to mean the preparation, deriving, compounding, propagation, processing, producing, or fabrication of a substance into a drug.[50]

Under the FDCA, a "manufacturer" is:
- A person who holds an application for a New Drug, Abbreviated New Drug, a Biologics License, or a New Animal Drug, approved under the federal act; or
- A person who holds a license issued under s. 351 of the Public Health Service Act, 42 U.S.C. s. 262, for such drug or biologics; or
- A person who manufactured the drug or biologics, not the subject of an approved application or license;
- A co-licensed partner of:
  - the holder of the drug application; or
  - the holder of the license, or
  - the manufacturer of the drug or biologics, not the subject of an approved application or license, who obtained the drug or biologics directly from the drug application holder license holder, or his or her affiliate;
- An affiliate of:
  - The holder of the drug application; or
  - The holder of the license, or
  - The co-licensed partner of the holder of the drug application; or
  - The co-licensed partner of the holder of the license; or
  - The co-licensed partner of the manufacturer of the drug or biologics, not the subject of an approved application or license, who receives the drug or biologics directly from the drug application or license holder, or the co-licensed partner; or
- A person who manufactures a device or cosmetic.[51]

Stem cells recovered, processed, and implanted in Florida that fit the above definitions are "unapproved new drugs" under both federal and state regulation and require a manufacturing

recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary or any supplement to any of them.

[49] Section 499.003(17), F.S.

[50] Section 499.003(28), F.S.

[51] Section 499.003(29), F.S.

permit issued by the DBPR to ensure the drugs are manufactured in accordance with good manufacturing practices.[52]

The FDCA defines the "distribution" of a drug to include the selling, purchasing, trading, delivering, handling, storing, or receiving of a drug; but does not include the administration or dispensing of a drug.[53]

Stem Cell Implantation or Transplantation

Stem cells may be collected, processed, and implanted or transplanted in a physician's office, health care clinic, ambulatory surgical center, or hospital.[54] In order to ship, mail, or deliver, in any manner, a medicinal drug into Florida, a nonresident pharmacy must be registered under s. 465.0156, F.S. In order to ship, mail, deliver, or dispense, in any manner, a compounded sterile product into Florida, a nonresident pharmacy, or an outsourcing facility, must hold a nonresident sterile compounding permit issued by the Board of Pharmacy (BOP).[55]

Physician's Office

The DOH Office of Surgery Registration and Inspection Program was established to register and set standards for allopathic and osteopathic physicians performing surgery in an office setting. The DOH requires all physicians who perform the following to register their office with the DOH:

- Liposuction procedures where more than 1,000 cubic centimeters of supernatant fat is removed;
- Level II procedures; and
- All Level III surgical procedures.[56]

Each registered physician's office must establish financial responsibility[57] and designate a physician who is responsible for the office's compliance with the office health and safety requirements. The designated physician must have a full, active, and unencumbered license and must practice at the office for which he or she is responsible. Within ten days after the termination of the designated physician, the office must notify the DOH of the designation of another physician to serve as the designated physician. If the office fails to comply with these requirements the DOH may suspend the registration.[58]

The DOH will inspect registered physicians' offices that are not nationally accredited, to ensure the safety of the people of Florida.[59]

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[52] Department of Business and Professional Regulation, Division of Drugs, Devices and Cosmetics, *Does my company need a permit? available at* http://www.myfloridalicense.com/DBPR/drugs-devices-and-cosmetics/do-i-need-a-license/#1508505246226-7153ba5b-b4c4 (last visited Jan. 31, 2020). See also s. 499.003(28), F.S.
[53] Section 499.003(16), F.S.
[54] See sections 395.002, 458.328, 459.0138, and 400.9935, F.S.; Fla. Adm. Code R. 64B8-9.009, and 64B15-14.007 (2019).
[55] Section 465.0158, F.S.
[56] Sections 458.328 and 459.0138, F.S.; Fla. Adm. Code R. 64B8-9.009, and 64B15-14.007 (2019).
[57] Section 458.328(1)(c), F.S.
[58] Section 458.328 (1)(b), F.S.
[59] The Department of Health, Licensing and Regulation, *Office Surgery Registration*, http://www.floridahealth.gov/licensing-and-regulation/office-surgery-registration/index.html (last visited Jan. 31, 2020).

Health Care Clinics

The Health Care Clinic Act[60] provides the Agency for Health Care Administration (AHCA) with licensing and regulatory authority to provide standards and oversite for health care clinics.[61] A clinic is defined as an entity where health care services are provided and which tenders charges for reimbursement for such services. Numerous exceptions to licensure exist.[62]The AHCA interprets the scope of its regulatory powers to solely include entities that bill third parties, such as Medicare, Medicaid, and insurance companies. Entities that provide health care services and accept "cash only" for services are excluded from the definition of "clinic" and are not subject to licensure or regulation by the AHCA.[63]

Hospitals and Ambulatory Surgical Centers

The AHCA is responsible for licensing, registering, and regulating hospitals and ambulatory surgical centers (ASC) pursuant to ch. 395, F.S. An ASC is a facility, the primary purpose of which is to provide elective surgical care, in which the patient is admitted to and discharged from such facility within 24 hours, and which is not part of a hospital.[64]

Regulation of Physicians in Florida

The BOM and the BOOM (the boards) within the DOH have the authority to adopt rules to regulate the 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.[65] 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.[66]

Currently, the BOM is warning physicians and consumers that they should be aware of the risks involved in stem cell therapies and regenerative medicine that have not been FDA-approved.[67] Although certain stem-cell therapies offer hope and hold great potential in treating devastating conditions, the FDA has approved few treatments involving stem cells. The BOM warns physicians providing stem cell treatment that he or she should have an investigational new drug application (IND) or a single patient IND for Compassionate or Emergency Use.[68] Florida does not specifically regulate clinics that perform treatments using stem cells, but the Boards have authority to investigate and discipline physicians who fail to meet the standard of care for providing any medical services.

[60] Part X of ch. 400, F.S.
[61] Section 400.990, F.S.
[62] Section 400.9905(4). F.S.
[63] Id.
[64] Section 395.002(3), F.S.
[65] Sections 458.331(v) and 459.015(z), F.S.
[66] *Id*.
[67] The Department of Health, Board of Medicine, *Information on Stem Cell Clinics Offering Unapproved Therapies*, http://flboardofmedicine.gov/latest-news/october-2015-newsletter/ (last visited Jan. 31 2020).
[68] *Id*.

In 2013, the BOM revoked the license of a physician who's administration of processed bone marrow cells, as "stem cell therapy," to a patient which caused the patient to die of a brain embolism.[69]

The U.S. Department of Justice, on behalf of the FDA, brought suit against a stem cell clinic located in Florida. In *United States of America vs. U.S. Stem Cell Clinic LLC*, 403 F.Supp.3d 1279 (2019), the U.S. District Court granted summary judgment and a permanent injunction requiring the defendant's stem cell business to stop advertising and marketing stem cell treatments which had been associated with severe complications in patients, including loss of sight. The court, in its opinion rendered on June 3, 2019, held that individual stromal and vascular stem cells, known as the "stromal vascular fraction" (SVF), used in the defendant's stem cell therapy, involved the removal of the SVF from a patient's cells and implanting the SVF alone back in same patient, after subjecting the patient's adipose cells to a specific and complex multi-step procedure, thereby creating a "drug" under the FDCA. The defendant further advertised and intended the SVF for use in the treatment of, inter alia, Parkinson's disease, stroke, and lung disease in humans. Thus, the SVF was subject to the FDCA's adulteration and misbranding provisions as a drugs regulated by the FDA, and the defendant's practices had not been approved by the FDA.[70]

The administration of stem cells as an adulterated drug continues to cause injury to Florida residents. On December 18, 2019, the Board of Medicine issued a final disciplinary order restricting the license of a physician for administering adipose tissue cells, as "stem cell therapy," into the eyes of a patient to treat her macular degeneration, which caused the patient to be blinded in one eye, and severely worsened the vision in her other eye.[71]

III. Effect of Proposed Changes:

SB 512 creates s. 381.4017, F.S., relating to nonembryonic stem cells and stem cell bank registration. The bill contains legislative finding that access to safe and high-quality health care services and products is of concern to all persons and regenerative medicine, including the use of nonembryonic stem cells, is a promising area of health care.

The bill defines the following terms:

- "Allogeneic" to mean originating from the body of another person;
- "Autologous" to mean originating from a person's own body;
- "Nonembryonic stem cells" to mean autologous or allogeneic cellular material that:
  - Has not been isolated or obtained directly from human embryos; and
  - May have been or may be combined with one or more:
    - Naturally occurring biomaterials; or
    - Materials approved or cleared by the FDA or other applicable agency or authority.

This definition would include all types of cellular material including skin grafts, bone marrow, and other types of human tissue.

[69] See *Department of Health vs. Zannos G. Grekos, M.D.*, Final Order, DOAH Case No. 11-4240PL, May 5, 2013; and
[70] *United States of America vs. U.S. Stem Cell Clinic LLC*, 403 F.Supp.3d 1279(2019).
[71] See *Department of Health vs. Shareen Mishal Greenbaum, M.D.*, Board of Medicine Final Order, DOH Case No.19-1922-S-MQA, December 18, 2019.

The bill defines an "independent third party" to mean an organization that provides:
- Industry safety standards;
- Relevant research;
- An industry-specific database in association with one or more stem cell banks; and
- Whose members are registered with the DOH.

The DOH must adopt rules for the development of the standards by an independent third party to ensure public safety and to implement the bill.

The bill provides that nonembryonic stem cells may be administered to a person by:
- Himself or herself; or
- A person licensed or authorized to administer or assist in the administration of medicine or health care, if that person administers or assists using a mode of administration permitted under his or her license or authorization.

The bill provides that a "health care product" may be compounded using nonembryonic stem cells as a sterile ingredient, either by themselves or in combination with other sterile ingredients. A pharmacy that compounds a drug, medicine, or health care product using nonembryonic stem cells may be owned or operated in this state and would require a community pharmacy permit under s. 465.018, F.S.

The bill provides that a person may import any sterile compound, drug, or other treatment containing nonembryonic stem cells if such compound, drug, or other treatment:
- Was obtained without violating the laws of the jurisdiction in which it was obtained; and
- Is for personal use.

The bill appears to allow any person to import sterile compound, drug, or other treatment containing nonembryonic stem cells and does not limit the jurisdictions from which such products may be obtained. Importation from other countries may require appropriate permits from the U.S. Customs and Border Patrol.

The bill provides that, notwithstanding any other provision of law, a stem cell bank may operate in Florida. Before organizing or arranging for the operation of a stem cell bank, a stem cell bank must register with the DOH by submitting a DOH-approved registration form that contains:
- The name, street address, and telephone number of the stem cell bank.
- The name, street address, and telephone number of each officer, director, or organizational official of the stem cell bank who is responsible for the operation of the stem cell bank.
- Identification of the types of human tissue used in business or research at the stem cell bank.
- Identification of the product names produced at the stem cell bank for distribution.
- Any other information required for registration by the DOH.

The bill requires that each stem cell bank obtain and carry, before engaging in such business, a professional liability insurance policy that insures the stem cell bank against any liability arising from its operation.

The bill also provides that it does not absolve:

- A professional licensing board of the duty to regulate licenses or otherwise prohibit or limit the powers and duties of a licensing board to regulate the procedures used to administer nonembryonic stem cells; or
- Any person of civil or criminal liability or penalty for failure to use the reasonable care, skill, or knowledge ordinarily used in rendering health care services or administering health care products under similar circumstances.

The bill provides an effective date of July 1, 2020.

IV. Constitutional Issues:

A. Municipality/County Mandates Restrictions:

None.

B. Public Records/Open Meetings Issues:

None.

C. Trust Funds Restrictions:

None.

D. State Tax or Fee Increases:

None.

E. Other Constitutional Issues:

None.

V. Fiscal Impact Statement:

A. Tax/Fee Issues:

None.

B. Private Sector Impact:

None.

C. Government Sector Impact:

The DOH reports that it will experience a recurring increase in workload and costs associated with the registration of stem cell banks and will incur non-recurring cost associated with third party rulemaking.[72]

[72] Department of Health, Senate Bill 512 Analysis (Jan. 23, 2020) (on file with the Senate Committee on Health Policy).

VI. Technical Deficiencies:

None.

VII. Related Issues:

The bill does not define the following terms:
- Cellular material;
- Naturally occurring biomaterials;
- Health care product; or
- Other sterile ingredients.

The bill requires a stem cell bank to register with the DOH. However, under current law, health care facilities are regulated by the AHCA, not the DOH. The bill gives the DOH no authority to deny such registration or to sanction registered stem cell banks that fail to operate within rules designed to ensure public safety.

The bill does not specify whether health care services may be provided at a stem cell bank facility. The bill defines "stem cell bank" to mean a facility that stores nonembryonic stem cells. The FDA defines a nonembryonic stem cell as a drug, and s. 499.003(18), F.S., defines the storage of a drug to be "distribution" but does not include the administration or dispensing of a drug. It is unclear how the stored stem cells are to get to a person to be administered, and, because they are being administered by a person who "administers medication or health care," the stem cell bank may, by default, be deemed a health care clinic under s. 400.9905(4), F.S.

The bill requires the DOH to adopt by rule the standards for stem cell banks developed by an independent third party and describes what constitutes such a third party. The bill does not specify how the DOH may identify or select the third party. The bill provides no parameters governing how the standards must be developed by the third party or what the specific objectives of the standards should be.

The bill requires that a stem cell bank must register with the DOH "before organizing or arranging for the operation of a stem cell bank." It is unclear how a stem cell bank can register before organizing itself.

The bill requires that each stem cell bank must obtain and carry, before engaging in such business, a professional liability insurance policy that insures the stem cell bank against any liability arising from its operation, but does not specify a required amount of coverage.

VIII. Statutes Affected:

This bill creates section 381.4017 of the Florida Statutes.

IX. Additional Information:

A. Committee Substitute – Statement of Changes:
(Summarizing differences between the Committee Substitute and the prior version of the bill.)

None.

B. Amendments:

None.