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:	CS/SB 512
INTRODUCER:	Health Policy Committee and Senator Hutson
SUBJECT:	Nonembryonic Stem Cells
DATE:	February 5, 2020 REVISED:

	ANALYST	STAFF DIRECTOR	REFERENCE	ACTION
1.	Rossitto-Van Winkle	Brown	HP	**Fav/CS**
2.			AP	
3.			RC	

Please see Section IX. for Additional Information:

COMMITTEE SUBSTITUTE - Substantial Changes

I. Summary:

CS/SB 512 defines multiple terms relating to the storing, making, and administering of nonembryonic stem cells. The bill treats nonembryonic stem cell banks (NSCBs) as health care clinics and requires them to:

- Register with the Agency for Health Care Administration (AHCA);
- Have a physician medical director who practices at the NSCB and is responsible for the NSCB complying with all requirements related to licensure, operation, and the good manufacturing practices requires under Florida and federal law;
- Maintain commercial and professional liability insurance in limits of minimum $250,000.

The bill authorizes an NSCB to:

- Make, collect, and store human nonembryonic stem cells and provide patient-specific health care services using human nonembryonic stem cells the NSCB manufactures;
- Sell and dispense nonembryonic stem cells manufactured by the NSCB, if the NSCB has a pharmacist, and is permitted as a pharmacy, to:
  - A health care practitioner to use in his or her office if the use is within the scope of the practitioner's license; and
  - Other stem cell banks, pharmacists, pharmacies, and establishments to sell or dispense to other health care practitioners if it is within the scope of practitioner's license to prescribe and administer human nonembryonic stem cells to patients.

The bill authorizes the Department of Health (DOH) to take disciplinary action against certain health care practitioners if found practicing in an unlicensed NSCB and requires the AHCA to make rules to administer NSCBs licensure and regulation, including specified topics to be included.

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* s. 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?* 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 ss. 395.002, 458.328, 459.0138, and 400.9935, F.S.; Rules 64B8-9.009 and 64B15-14.007, F.A.C. (2019).
[55] Section 465.0158, F.S.
[56] Sections 458.328 and 459.0138, F.S.; Rules 64B8-9.009 and 64B15-14.007, F.A.C. (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:

The bill defines a "nonembryonic stem cell," also referred to as a "somatic stem cell" or an "adult human stem cell," as an allogenic or autologous cell that is undifferentiated and unspecialized and that has the ability to divide for indefinite periods of time in a medium and to become a specialized cell. The term includes a human nonembryonic cell that is altered or processed to become undifferentiated, losing its original structural function, so that it can be differentiated into a specialized cell type. The term does not include cells that are minimally manipulated or are only rinsed, cleaned, or sized and remain differentiated.

The bill defines a NSCB as a publicly or privately owned establishment that does any of the following:

- Collects and stores human nonembryonic stem cells for use in a product or patient-specific medical administration;
- Provides patient-specific health care services using human nonembryonic stem cells;

[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.

- Advertises human nonembryonic stem cell services, including, but not limited to, collection, manufacturing, storage, dispensing, use, or purported use of human nonembryonic stem cells or products containing human nonembryonic stem cells, which:
  - Have not been approved by the United States Food and Drug Administration; or
  - Are not the subject of clinical trials approved by the United States Food and Drug Administration; and
  - Which are intended to diagnose, cure, mitigate, treat, provide therapy for, or prevent an injury or a disease.
- Performs any procedure that is intended to:
  - Collect or store human nonembryonic stem cells for any purpose; or
  - Diagnose, cure, mitigate, treat, provide therapy for, or prevent an injury or a disease with the use or purported use of human nonembryonic stem cells or any product containing human nonembryonic stem cells which has not been approved by the United States Food and Drug Administration or is not the subject of a clinical trial approved by the United States Food and Drug Administration.
- Compounds human nonembryonic stem cells from human nonembryonic cells or tissue into products by combining, mixing, or altering the ingredients of one or more drugs or products to create another drug or product;
- Manufactures, through recovery, processing, manipulation, enzymatic digestion, mechanical disruption, or a similar process, human nonembryonic stem cells from human nonembryonic cells or tissue into undifferentiated human nonembryonic stem cells, causing the cells to lose their original structural function so that the nonembryonic stem cells may be differentiated into specialized cell types; or
- Dispenses human nonembryonic stem cells and products containing nonembryonic stem cells to any of the following, for a specific patient pursuant to a valid prescription from a licensed health care practitioner authorized within the scope of his or her license to prescribe and administer human nonembryonic stem cells:
  - A pharmacy permitted under ch. 465, F.S.;
  - A health care practitioner with privileges to practice at nonembryonic stem cell banks; or
  - A health care practitioner's office, a health care facility, or a treatment setting where the health care practitioner has privileges to practice, for office use.

The bill also defines the following specific terms relating to the making, storing and administration of nonembryonic stem cells:

- Compounding - means combining, mixing, or altering the ingredients of one or more drugs or products to create another drug or product.;
- Dispense - has the same meaning as in s. 465.003(6), F.S.;
- Establishment - means a place of business which is at one general physical location and may extend to one or more contiguous suites, units, floors, or buildings operated and controlled exclusively by entities under common operation and control. The term includes multiple buildings with an intervening thoroughfare if the buildings are under common exclusive ownership, operation, and control. For purposes of permitting, each suite, unit, floor, or building must be identified in the most recent permit application;
- Federal Act - means the Food and Drug Administration Act, 21 U.S.C. ss. 301 et seq.; 52 Stat. 1040 et seq.;
- Minimally manipulated means:

  - For structural tissue, processing that does not alter the original characteristics of the tissue which relate to the tissue's utility for reconstruction, repair, or replacement; or
  - For cells or nonstructural tissue, processing that does not alter the relevant biological characteristics of the cell or tissue; and
- Office use means the provision and administration of a drug, compounded drug, or compounded product to a patient by a health care practitioner in the practitioner's office or in a health care facility or treatment setting, including a hospital, ambulatory surgery center, or health care clinic licensed under chapter 395 or chapter 400. The term also includes the dispensing by a pharmacist at a nonembryonic stem cell bank that is also permitted as a pharmacy under chapter 465 to a nonembryonic stem cell bank within this state of any of the following:
  - Human nonembryonic stem cells;
  - A compounded drug containing human nonembryonic stem cells; or
  - A compounded product containing nonembryonic stem cells..

The bill requires the NSCB to:

- Adhere to the current good manufacturing practices for the collection, removal, manufacturing, processing, compounding, and implantation of nonembryonic stem cells, or products containing them, under Florida law, the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. ss. 301 et seq.; 52 Stat. 1040 et seq.; and 21 C.F.R., parts 1270-1271;
- Obtain a health care clinic license and register each establishment separately, unless:
  - The clinic is a facility licensed under chapter 395; or
  - The clinic is affiliated with an accredited medical school that provides training to medical students, residents, or fellows.
- Have a physician medical director, a full, active, and unencumbered license, who actively practices at the NSCB, and who is responsible for the NSCB's compliance with all licensure, operations and good manufacturing practices requirements;
- Notify the AHCA, in writing, on a form approved by the AHCA within 10 days after termination of a physician medical director; and notify the AHCA within 10 days after such termination of the identity of the new physician medical director who has assumed the responsibilities for the NSCB. Failure to have a physician medical director practicing at the location of the NSCB is a basis for a summary suspension of the NSCB's license pursuant to s. 400.607 or s. 120.60(6), F.S.;
- Maintain commercial and professional liability insurance in an amount not less than $250,000 per claim;
- Operate each establishment using the same name as the one used to obtain the health care clinic license; and requiring all invoices, packing slips, and other business records to list the same name;
- Obtain a pharmacy permit for each person and establishment before dispensing, offering office use for the compounding of human nonembryonic stem cells, or dispensing a compounded product for office use; and
- Pay all costs associated with licensure, registration and inspection.

The bill authorizes a pharmacist at a NSCB, with a pharmacy permit, to dispense human nonembryonic stem cells, a compounded drug containing human nonembryonic stem cells; and

a compounded product containing human nonembryonic stem cells to another NSCB within the state, for office use.

The bill prohibits the sale or dispensing of human nonembryonic stem cells, a compounded drug containing human nonembryonic stem cells; or a compounded product containing human nonembryonic stem cells by any person or establishment, other than the NSCB or pharmacist at the NSCB that manufactured the human nonembryonic stem cells, the compounded drug, or product containing human nonembryonic stem cells, except that:

- A health care practitioner who requests the dispensing of the human nonembryonic stem cells, compounded drug, or compounded product from the manufacturing NSCB may sell or dispense such items to his or her patient if the health care practitioner is authorized within the scope of his or her license to prescribe and administer human nonembryonic stem cells; or
- A pharmacist, pharmacy, or establishment that requests the dispensing of the human nonembryonic stem cells, compounded drug, or compounded product from the manufacturing NSCB may sell or dispense such items to a health care practitioner who is authorized within the scope of his or her license to prescribe and administer human nonembryonic stem cells to patients.

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:

CS/SB 512 requires a NSCB to register with the AHCA as a health care clinic, to maintain commercial and professional liability insurance in an amount not less than $250,000 per claim, and to pay all costs associated with licensure, registration and inspection. These additional costs may result in an increase in the costs of NSCB's services to consumers.

C. Government Sector Impact:

The AHCA may experience a recurring increase in workload and costs associated with the registration of NSCBs as health care clinics.

VI. Technical Deficiencies:

None.

VII. Related Issues:

None.

VIII. Statutes Affected:

This bill creates section 381.06017 of the Florida Statutes.

IX. Additional Information:

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

CS by Health Policy on February 4, 2020:
The CS:

- Creates s. 381.06017, F.S., rather than s. 381.4017, F.S., which authorizes NSCB's to operate in Florida;
- Requires NSCBs to register with the AHCA as a health care clinic, rather than the DOH;
- Defines an NSCB broadly, not just a facility that stores nonembryonic stem cells, but as any establishment that:
  - Manufactures, collects, or stores human embryonic stem cells;
  - Provides patient-specific health care services using human nonembryonic stem cells;
  - Advertises human nonembryonic stem cell services;
  - Preforms procedures that:
    1) Collects or stores human embryonic stem cells; or
    2) Use non-FDA approved human nonembryonic stem cells, alone, or as a compounded drug or product, to diagnose, cure, treat, provide therapy for, or to prevent injury or disease; or
  - Compounds human nonembryonic stem cells into a compounded drug or product.

- Authorizes the administration of nonembryonic stem cells only by health care practitioners that the scope of the practitioner's license permits the prescribing and administering of human nonembryonic stem cells; and does not authorize:
  - The self-administration of nonembryonic stem cells; or
  - The administration of nonembryonic stem cells by just any person licensed or authorized to administer, or assist in the administration of, medications or health care;
- Does not authorize every pharmacy, owned or operated in Florida, to compound health care products using nonembryonic stem cells either alone or with other sterile ingredients.
- Does not authorize 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.
- Requires the NSCB to carry both commercial and liability insurance in an amount not less than $250,000 per claim, where the original bill did not specify limits; and
- Authorizes the AHCA to adopt rules necessary to administer the licensure and regulation of NSCBs.

B. Amendments:

None.