



Regenerative and Stem Cell Therapy Practices

Report and Recommendations of the Workgroup to Study Regenerative and Stem Cell Therapy Practices

*Adopted as policy by the Federation of State Medical Boards
April 2018*

Section One. Introduction and Charge:

The Federation of State Medical Boards (FSMB) Workgroup to Study Regenerative and Stem Cell Therapy Practices was convened in May of 2017 by FSMB Chair Gregory B. Snyder, M.D., DABR, in response to a letter (Attachment 1) from U.S. Senator Lamar Alexander (R-TN), Chairman of the U.S. Senate Health, Education, Labor, and Pensions (HELP) Committee, urging the FSMB to develop best practices for state medical and osteopathic boards (hereinafter referred to as “state medical boards”) in regulating the promotion, communication, and practices of treatments received at stem cell clinics in the United States.

In order to address Senator Alexander’s request, Dr. Snyder charged the Workgroup with:

- 1) Evaluating the prevalence, promotional practices, and incidences of patient harm related to regenerative medicine and adult stem cell therapies in the U.S.;
- 2) Evaluating current regulatory approaches that will protect the public, recognizing the potential for improved patient outcomes through health innovation and technology;
- 3) Identifying best practices for state medical and osteopathic boards in investigating complaints of patient harm, fraud, and compliance with licensure requirements; and
- 4) Issuing a report on the Workgroup’s findings from prevailing research and recommending best regulatory practices and guidelines related to physicians’ use of regenerative medicine and adult stem cell therapies in a manner consistent with safe and responsible medicine.

Stem cell and regenerative therapies offer opportunities for advancement in the practice of medicine and the possibility of an array of new treatment options for patients experiencing a variety of symptoms and conditions. Despite significant momentum in research and development, and the potential for such medical advancements, there is reasonable concern about a growing number of providers and clinics in the United States that are undermining the field. Such providers and clinics have been known to apply, prescribe or recommend therapies inappropriately, over-promise without sufficient data to support claims, and exploit patients who are often in desperate circumstances and willing to try any proposed therapy as a last resort, even if there is excessive cost or scant evidence of efficacy.

The following report aims to raise awareness about regenerative and stem cell therapy practices generally, outline their potential benefits and risks, and provide basic guidance for state medical boards and licensed physicians and physician assistants. Central to all of the recommendations provided herein is a range of imperatives, including the importance of protecting the public, respecting patient autonomy, preventing patient exploitation, obtaining informed consent, and appropriately documenting care that is recommended and provided.

The Workgroup's deliberations were aided by participants and subject matter experts who brought varying perspectives. For example, Dr. Ronald Domen has expertise in stem cell therapies, bioethics and humanities, and has served on numerous ethics committees at institutional, state, and national levels. Dr. Zubin Master of the Mayo Clinic has extensive training and education in cellular and molecular biology, bioethics and genetics, as well as research and publications on stem cell therapies. Mr. Douglas Oliver became known to the Workgroup through a recommendation by Senator Lamar Alexander of Tennessee, was a recipient of stem cell therapies himself, and has a foundation that advocates for stem cell therapies based on his own experiences and those of others like him. Dr. Bruce White has educational backgrounds in medicine, law, pharmacy and ethics and currently serves as Director of the Alden March Bioethics Institute at Albany Medical College and is Chair of Medical Ethics at the College. The Workgroup also received written comments from several external organizations. The sum of these perspectives aided the Workgroup in producing a balanced report on this emerging issue of national importance.

Section Two. Definitions:

Homologous (Allogeneic) Use: the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with a HCT/P (human cells, tissues, and cellular and tissue-based product) that performs the same basic function or functions in the recipient as in the donor, including when such cells or tissues are for autologous use.¹

According to the Food and Drug Administration's (FDA) *Regulatory Considerations for Human Cell, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use / Guidance for Industry and Food and Drug Administration Staff (November 2017)*, the FDA "generally considers an HCT/P to be for homologous use when it is used to repair, reconstruct, replace, or supplement:

- Recipient cells or tissues that are identical (e.g., skin for skin) to the donor cells or tissues, and perform one or more of the same basic functions in the recipient as the cells or tissues performed in the donor; or
- Recipient cells or tissues that may not be identical to the donor's cells or tissues, but that perform one or more of the same basic functions in the recipient as the cells or tissues performed in the donor."²

¹ 21 CFR 1271.3(c)

²U.S. Food and Drug Administration (November 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*.

Autologous Use: the implantation, transplantation, infusion, or transfer of human cells or tissue back into the individual from whom the cells or tissue were recovered.³

Informed and Shared Decision Making: The process by which a physician discusses, in the context of the use of regenerative and stem cell therapies, the risks and benefits of such treatment with the patient.⁴ The patient is given an opportunity to express preferences and values before collaboratively evaluating and arriving at treatment decisions.⁵

Informed Consent:⁶ Evidence documenting appropriate patient informed consent typically includes the following elements:

- Identification of the patient, the physician, and the physician’s credentials;
- Types of transmissions permitted using regenerative and stem cell therapies (e.g. prescription refills, appointment scheduling, patient education, etc.);
- Agreement from the patient with the physician’s determination about whether or not the condition being diagnosed and/or treated is appropriate for regenerative and stem cell therapy;⁷ and
- Express patient consent to forward patient-identifiable information to a third party
- An accurate description of the benefits and risks of treatment or intervention, based on scientific evidence, as well as an explanation of alternatives to treatment or an intervention, and the right to withdraw from treatment or an intervention without denial of standard of care to patients.

Minimal Manipulation: (minor processing including purification, centrifugation, washing, preservation, storage) – the Food and Drug Administration (FDA) argues that it has the authority to regulate anything beyond minimal manipulation and homologous use:

“(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; and
(2) For cells or nonstructural tissues, processing that does not alter the relevant biological characteristics of cells or tissues.”⁸

Unproven Stem Cell Intervention: Stem cell therapy that lacks compelling evidence, based upon scientific studies, to validate its treatment efficacy.⁹

³ 21 CFR 1271.3(a)

⁴ Federation of State Medical Boards (2016). Model Guidelines for the Recommendation of Marijuana in Patient Care.

⁵ Barry, MJ, Edgman-Levitan, S. (2012). Shared Decision Making – The Pinnacle of Patient-Centered Care. *N Engl J Med*, 366:780-781.

⁶ With respect to informed consent for the purposes of research studies involving human subjects, researchers should be aware of the basic elements of informed consent outlined in 21 CFR Part 50.25 “Protection of Human Subjects.”

⁷ Federation of State Medical Boards (2014). Model Policy for the Appropriate Use of Telemedicine Technologies in the Practice of Medicine.

⁸ 21 CFR 1271.3(f)

⁹ Sipp D, et al. (2017). Marketing of Unproven Stem Cell-Based Interventions: A Call to Action. *Science Translational Medicine*, 9:397.

Section Three. Background, Prevalence and Marketing of Regenerative and Stem Cell Therapies:

Historically, many of the clinics providing unproven stem cell interventions fell under the definition of “stem cell tourism” because most patients seeking such interventions had to travel outside of North American jurisdictions to receive them. The landscape in the United States has evolved considerably over the last few years with hundreds of new clinics opening across the country and many more physicians willing to provide stem cell and regenerative therapies. A study identified 351 U.S. businesses with over 570 clinics engaged in direct-to-consumer (DTC) marketing of stem cell interventions.¹⁰ It has also been suggested that growth in this area of medicine, especially in terms of adult, amniotic, fat-derived and bone marrow stem cell therapies to treat a host of conditions and injuries, is accelerating, both in the U.S. and internationally, and, perhaps counterintuitively, such growth is noted to be most significant in jurisdictions with more stringent regulatory frameworks.¹¹

Stem cell clinics typically reach their patients through online DTC marketing, primarily through information provided on company websites. Data purportedly supporting unproven stem cell interventions commonly undermine information about risks and overemphasize information about benefits. Treatment options are described on such websites and are often accompanied by supporting information in the form of journal articles, patient testimonials, and accolades related either to the clinic itself or its affiliated physicians and researchers. Supporting information that accompanies marketing materials can appear to be legitimate, but can also overemphasize, exaggerate, inflate, or misrepresent information derived from legitimate (or even questionable) sources. A physician engaging in such practices of deceptive or false advertising can be in violation of a state’s *Medical Practice Act*. Information provided on clinic websites should be represented accurately and come from reputable peer-reviewed publications or respected external organizations.

Some clinics, however, that are engaged in the provision of treatment modalities that lack evidence – or an appropriate rationale for application of that modality to particular medical conditions – often use what have been described as “tokens of scientific legitimacy” to lend credence to treatments offered or the quality of a clinic and its associated professionals. Examples of such tokens of legitimacy include patient or celebrity testimonials and endorsements, clinician affiliations or memberships in academic or professional societies, registrations in clinical trials, claims of various types of certifications or awards, and others.¹² Further detail and explanations are provided in **Table 1**.

Physicians are ordinarily permitted to advertise themselves, their practice and services offered, provided that such advertisements do not contain claims that may be deceptive or are intentionally false or misleading. Further, physicians should be mindful of ways in which patient

¹⁰ Turner L, Knoepfler P. (2016). Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry *Cell Stem Cell* 19, August 4, 154-7.

¹¹ Berger, et al. (2016) Global Distribution of Businesses Marketing Stem Cell-Based Interventions. *Cell Stem Cell* 19, August 4, 158-62.

¹² Sipp D, et al. (2017). Marketing of Unproven Stem Cell-based Interventions: A Call to Action. *Sci. Transl. Med.* 9, eaag0426.

testimonials, quality ratings, or other evaluative data is presented to prospective patients through advertisements. In advertising stem cell treatments to potential patients, physicians are responsible for ensuring that all information, especially in terms of risks, benefits and efficacy, is presented in an objective manner. Physicians must not deliberately misrepresent the expected outcomes or results of treatments offered. Physicians should be prepared to support any claims made about benefits of treatment(s) with documented evidence, for example with studies published in peer-reviewed publications.¹³

Physicians must be accurate and not intentionally misleading in providing descriptions of their training, skills, or treatments they are able to competently offer to patients. This includes descriptions of one's specialization and any specialty board certifications.¹⁴

A recent study on the prevalence and marketing practices of businesses offering stem cell treatments internationally noted the presence of the following elements in their marketing practices:

- Mention of affiliations with a professional society or network
- Claims of partnerships with academic institutions
- Statements of receipt of FDA approval, or explicit mention of exemption from FDA oversight
- Mention of official endorsement from a local or other authority, or professional accreditation
- Listing of patents granted
- Statement that clinical trials of investigational stem cell-based interventions are being conducted¹⁵

The marketing practices and information found on a business' website can be important sources of data for state medical boards as they investigate complaints made against physicians affiliated with businesses providing regenerative and stem cell treatments. Even where an appropriate informed consent process seems to be in place, deceptive or fraudulent information on clinic websites and other marketing materials could mislead patients into consenting to treatment, thereby invalidating the informed consent process.

Physicians must make accurate claims about the enrollment process of subjects, treatments, and products in clinical trials and are responsible for ensuring that any research conducted and described in marketing materials is carried out according to accepted research protocols and recognized standards. Physicians should consider consulting with Institutional Review Boards (IRBs) to clarify processes and must seek IRB approval, where necessary. The National Institutes of Health (NIH) provides helpful guidance on clinical trials and research methods.¹⁶ Physicians are also encouraged to consult the guidance contained in the *International Conference*

¹³ Federation of State Medical Boards (2016). *Position Statement on Sale of Goods by Physicians and Physician Advertising*.

¹⁴ *Ibid.*

¹⁵ Berger, et al. (2016) Global Distribution of Businesses Marketing Stem Cell-Based Interventions. *Cell Stem Cell* 19, August 4, 158-62.

¹⁶ National Institutes of Health, Office of Science Policy: <https://osp.od.nih.gov/clinical-research/clinical-trials/>

on Harmonisation’s Harmonised Tripartite Guideline for Good Clinical Practice to support acceptability of clinical data by patients, state medical boards, and other regulatory authorities.¹⁷

Table 1: Co-opted Tokens of Scientific Legitimacy¹⁸

Accreditations and awards	Asserting certification of products or practices by international standards organizations or claiming training certification
Boards and advisers	Convening scientific or medical advisory boards featuring prominent business leaders and academic faculty members
Clinical study registration	Registering trials whose apparent purpose is solely to attract patients willing to pay to participate in them
Ethics review	Using the imprimatur of “ethics review” to convey a sense of legitimacy to their products or procedures
Location	Renting of laboratory or business space within a legitimate scientific or government institution
Membership	Joining established academic or professional societies to suggest legitimacy by association
Outcome registries	Publication of open-ended voluntary monitoring data sets rather than undertaking controlled clinical trials
Patenting	Suggesting that patent applications or grants indicate clinical utility rather than initiation of an application process or recognition of novelty and inventiveness
Publication	Publishing research and commentary in journals with limited anonymous peer review
Rationales	Citing preclinical and other research findings to justify clinical application without sufficient efficacy testing in humans
Self-regulation	Forming organizations to self-regulate in ways that support premature commercialization
Technical Language	Using scientific-sounding words that imply academic rigor
Testimonials and Endorsements	Providing expert opinions or celebrity comments on unsupported clinical uses or standing of the provider

Section Four. Patient Perceptions:

In seeking treatment for any condition, patients desire safety and efficacy, but may overlook risks to their own safety or a lack of evidence of efficacy in favor of access to treatment, particularly in circumstances where traditional treatment options seem limited or have been exhausted. The power of hope also is known to play a significant role in how patients attempt to gain control over their illness and its potential treatments, thereby putting them in a position of

¹⁷ International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. (2016). ICH Harmonised Tripartite Guideline for Good Clinical Practice E6(R2).

¹⁸ Sipp D, et al. (2017). Marketing of Unproven Stem Cell-based Interventions: A Call to Action. *Sci. Transl. Med.* 9, eaag0426.

increased vulnerability.¹⁹ This is especially the case when patients and their families have overcome various obstacles on the path to a treatment, including raising large sums of money to pay for it. This can lead to a psychological predisposition to anticipate and assume a positive outcome, regardless of the treatment in question or the availability of compelling evidence.

Given the vulnerable state of some patients who seek regenerative and stem cell therapies, perhaps without the requisite knowledge for making informed decisions, there is increased potential for patient exploitation. Physicians must therefore be mindful of the ways in which at-risk or susceptible patients may process information and arrive at decisions about their treatment options, expectations, and ultimately, the potential for success. A promising way of navigating such difficult circumstances, where treatment options are uncertain or complex, is through the use of shared decision making. This process, whereby the physician describes the risks and benefits of potential treatment options and the patient is given an opportunity to express preferences and values before collaboratively arriving at and evaluating treatment decisions,²⁰ may help mitigate the risk of patient exploitation and ensure that consent to any treatment option has been provided in an informed manner.

The process of obtaining informed consent and engaging in shared decision making with patients involves conveying information about the reasonable effectiveness of a proposed treatment, as well as its risks and benefits. This can be particularly difficult with respect to regenerative and stem cell therapies, as this is an area of medicine that currently lacks substantive data on efficacy. Generation of relevant data and evidence has not occurred to a sufficient enough degree and this is often blamed on the difficulty involved in organizing large-scale, randomized controlled trials as part of the approval process for novel therapies. However, the FDA has recently argued that a statistically significant 100% improvement in an outcome measure ($\alpha = 0.05$, $\beta = 0.1$) may be detected with a randomized trial involving as few as 42 participants.²¹

The lack of a formal mechanism for reporting outcomes of unproven stem cell interventions, both positive and negative, adds to the difficulty involved in generating data on the effectiveness of such interventions, as does the fact that there is neither a requirement, nor a mechanism, for reporting adverse events related to interventions administered outside of clinical trials and investigations. In the current environment, this increases the importance of appropriate documentation of treatment(s) and ongoing care in patients' medical records. A centralized cell therapy registry for reporting treatment and outcomes may improve the current information available about the effectiveness of such therapies and interventions. It may also dissuade unscrupulous practitioners from engaging in the provision of unproven interventions without an adequate or appropriate basis in theory or peer-acknowledged practice, a pre-requisite for the provision of any intervention, whether proven or not.²²

¹⁹ Petersen, et al. (2014). Therapeutic Journeys: The hopeful travails of stem cell tourists, *Sociology of Health & Illness*, 36(5):670-85, pp. 1–16.

²⁰ Barry, MJ, Edgman-Levitan, S. (2012). Shared Decision Making – The Pinnacle of Patient-Centered Care. *N Engl J Med*, 366:780-781.

²¹ Marks PW, et al. (2017). Clarifying Stem-Cell Therapy's Benefits and Risks, *NEJM* 376;11, 1007-9.

²² White, BD, Gelinas, LC, (2016). "Balancing the Surgeon's Responsibility to Individuals and Society," published in S.C. Stain et al. (eds.), *The SAGES Manual Ethics of Surgical Innovation*, Switzerland: Springer International Publishing, 191-211.

Section Five. Regulatory Landscape:

The current state of affairs for regulatory oversight on regenerative and stem cell therapies (including human cells and tissues), at both the federal and state level, is evolving and will continue to change in the coming years. In November 2017, the FDA released two guidance documents to explain the Agency’s current thinking on stem cell policy. However, this thinking, as well as the agency’s jurisdiction and authority, may evolve in the future.

Until recently, the regulatory landscape for stem cell and regenerative therapies has been at times restrictive, allowing patients to access stem cell interventions only under the *Expanded Access to Investigational Drugs for Treatment Use* program. Treatments are eligible under this program if they are undergoing testing in a clinical trial and are subject to approval by the FDA. Three-quarters of the states in the nation have passed “Right to Try” legislation, however, which allows terminally ill patients to receive experimental therapies that have passed phase 1 trials without seeking FDA approval.²³ The U.S. Congress is also considering similarly proposed legislation and in August of 2017, the U.S. Senate passed *S. 204, Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017*.

The *21st Century Cures Act* (Public Law 114–255), signed into law in December of 2016, represents legislative efforts at the federal level to expand and accelerate patient access to treatment, in addition to promoting innovation in medical products and treatments. With respect to regenerative medicine, the Act amends Section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356) by requiring expedited review for regenerative medicine therapies, including human cells and tissues, intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, where there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs. There are also ongoing efforts at the federal level to ensure even greater access to treatments that are not subject to FDA approval prior to administration to patients.

Regulation in the regenerative and stem cell therapy arena is continuing to evolve. Human cells, tissues, and cellular or tissue-based products (HCT/Ps) are currently regulated under Sections 351 and 361 of the Public Health Service Act.²⁴ However, a HCT/P can be regulated solely under Section 361 of the PHS Act if it is:

1. Minimally manipulated,
2. Intended for homologous use only,
3. Not combined with another article, and
4. Either:
 - a. Does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or

²³Lancet Commission: Stem Cells and Regenerative Medicine. Published Online October 4, 2017

[http://dx.doi.org/10.1016/S0140-6736\(17\)31366-1](http://dx.doi.org/10.1016/S0140-6736(17)31366-1)

²⁴ The Public Health Service Act of 1944 outlines a policy framework for federal and state cooperation in health services and provides for the licensing of biological products.

- b. Has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and is for autologous use, use in a first or second-degree blood relative, or reproductive use.²⁵

The difference between an HCT/P that is regulated under both sections of the Public Health Service Act, as opposed to solely under Section 361, is significant for providers of stem cell treatments since the requirements for pre-market authorization of a product are much more stringent under Section 351 and require conducting clinical investigations under an investigational new drug (IND) application and obtaining a biologics license through the FDA, whereas requirements under Section 361 focus only on the prevention of communicable diseases.²⁶ This represents a lower regulatory threshold for HCT/Ps; their use and transplantation can be considered to fall under the practice of medicine and would, therefore, be regulated by state medical boards.

In regulating this evolving area of medical practice, state medical boards will need to strive to achieve an appropriate balance between respecting the autonomy of patients as they seek viable and reasonable treatment options, and adequately safeguarding them against the risks presented by novel, but often unproven and potentially dangerous, interventions. Results from a 2017 survey of its member boards conducted by the FSMB indicate that a third (n = 17) of the 51 responding boards have investigated complaints against physicians related to regenerative medicine or stem cell therapy, and that eight of those boards have taken disciplinary action against physicians for issues relating to regenerative medicine or stem cell therapy.

In ensuring that physicians offer regenerative and stem cell therapies in a manner that is consistent with safe and responsible practices, state medical boards should ensure that any treatment offered to patients is informed by an appropriate history and physical examination; such informed consent is obtained after an explanation has been provided describing risks, benefits, alternative treatment options, expected convalescence, and expected treatment outcomes; that relevant information about the clinical encounter and ongoing care plans has been documented in the patient's medical record; that the physician is appropriately trained in, and knowledgeable about the proposed treatment; and that the patient has not been coerced in any way into receiving treatment(s) or exploited through the charging of excessive fees.

In order to implement best practices for regenerative and stem cell therapies, physicians must understand the relevant clinical issues and should obtain sufficient targeted continuing education and training.²⁷

The recommendations in the final section of this report provide further detail on various requirements that apply to the provision of regenerative and stem cell therapies that state medical boards may wish to consider.

²⁵ 21 CFR 1271.10(a)

²⁶ United States Food and Drug Administration: Regulatory Considerations for Human Cell, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use

²⁷ Federation of State Medical Boards (2017). *Guidelines for the Chronic Use of Opioid Analgesics*.

Section Six. Recommendations:

The recommendations that follow address the regulation of the provision of stem cell and regenerative therapies, as well as their promotion and communication to patients, and documentation of treatments provided. The recommendations do not address which uses are appropriate or not for specific conditions or symptoms, as this area of medicine continues to be dynamic and subject to change. Rather, they focus on sensible and necessary principles of patient safety, autonomy, and non-exploitation.

The FSMB recommends that:

1. Where evidence is unavailable for a particular treatment in the form of clinical trials or case studies, physicians must only proceed with an appropriate rationale for the proposed treatment, and justification of its use, in relation to the patient's symptoms or condition. Novel, experimental, and unproven interventions should only be proposed when traditional or accepted proven treatment modalities have been exhausted. In such instances, there must still be a basis in theory or peer-acknowledged practice.²⁸
2. State medical boards raise awareness among licensees of applicable federal and state legislation and guidelines regarding regenerative and stem cell therapies, including "right to try" legislation existing or pending at the state and federal levels. State medical boards should also keep their licensees and the public apprised of new developments and regulations in the field of regenerative and stem cell therapies. This may include educational resources, guidance documents, and appropriate industry and stakeholder information on a state medical board's website. State medical boards should further provide information as to reporting procedures of adverse actions related to stem cell interventions.
3. State medical boards should examine their policies and rules addressing informed consent and consider expanding these to include a shared decision making framework that includes the following general elements at a minimum:
 - An explanation, discussion, and comparison of treatment options with the patient
 - An assessment of the patient's values and preferences
 - Arrival at a decision in partnership with the patient
 - An evaluation of the patient's decision in partnership with the patient
4. State medical boards should review professional marketing materials and claims, including any office/clinic and/or doctor websites, and information publicly available about an office/clinic or licensee on online blogs or social media, as information sources in the investigation of complaints made against physicians.
5. State medical boards should pro-actively monitor warning letters sent to licensees that are made publicly available on the FDA website in order to ascertain information, and consider opening an investigation, about licensees who may be engaged in other unscrupulous or

²⁸ White, BD, Gelinas, LC, (2016). "Balancing the Surgeon's Responsibility to Individuals and Society," published in S.C. Stain et al. (eds.), *The SAGES Manual Ethics of Surgical Innovation*, Switzerland: Springer International Publishing, 191-211.

unprofessional practices related to the provision of regenerative and stem cell therapy. State medical boards should investigate such practices, when appropriate, in conjunction with applicable state laws, policies, and procedures.²⁹

6. Physicians must only offer treatments to patients for which they have a bona fide physician-patient relationship. Physicians must have received adequate and appropriate training, and be able to perform any proposed intervention safely and competently.³⁰

7. Physicians should employ a “shared decision making” process when discussing treatment options with patients. Physicians must avoid any claims that may be deceptive or are intentionally or knowingly false or misleading, especially in terms of making promises about uncertain or unrealistic outcomes.

8. Physicians should not use gag orders (rulings that a case must not be discussed publicly) or disclaimers as a way to circumvent liability.

9. Physicians should be prepared to support any claims made about benefits of treatments or devices with documented evidence, for example with studies published in peer-reviewed publications.

10. Physicians should refrain from charging excessive fees for treatments provided. Further, physicians should not recommend, provide, or charge for unnecessary medical services, nor should they make intentional misrepresentations to increase the level of payment they receive.³¹

11. Physicians should consult and educate patients about stem cell interventions and alert them to important resources available to the community. A list of selected resources is provided in **Appendix A**.

²⁹ The FDA’s warning letters are available at the following address:

<https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm>

³⁰ Federation of State Medical Boards (2014). *Model Policy for the Appropriate Use of Telemedicine Technologies in the Practice of Medicine*.

³¹ American Medical Association, *Code of Medical Ethics*, Opinion 11.3.1.

WORKGROUP TO STUDY REGENERATIVE AND STEM CELL THERAPY PRACTICES

Scott A. Steingard, DO, Chair
FSMB Director-at-Large
Past President, Arizona Board of Osteopathic Examiners in Medicine and Surgery

Debbie J. Boe
Former Public Member, Minnesota Board of Medical Practice

Sandra L. Coletta
Public Member, Rhode Island Board of Medical Licensure and Discipline

Sarah L. Evenson, JD, MBA
Former Public Member, Minnesota Board of Medical Practice

H. Joseph Falgout, MD
Chair, Alabama Board of Medical Examiners

Joseph E. Fojtik, MD, FACP
Deputy Medical Coordinator, Illinois Department of Financial & Professional Regulation

Gary R. Hill, DO
Member, Alabama Medical Licensure Commission

Howard R. Krauss, MD
Member, Medical Board of California

SUBJECT MATTER EXPERTS

Ronald E. Domen, MD, FACP, FCAP
Penn State College of Medicine

Zubin Master, PhD
Mayo Clinic

Douglas Oliver, MSW
Patient Appointee
Founder and Executive Director, Regenerative Outcomes Foundation

Bruce D. White, DO, JD
Alden March Bioethics Institute

EX OFFICIOS

Gregory B. Snyder, MD, DABR
Chair, FSMB

Patricia A. King, MD, PhD, FACP
Chair-elect, FSMB

Humayun J. Chaudhry, DO, MS, MACP, MACOI
President and CEO, FSMB

STAFF SUPPORT

Jonathan Jagoda, MPP
Director, Federal Government Relations, FSMB

Mark Staz, MA
Director, Continuing Professional Development

APPENDIX A: SAMPLE LIST OF EDUCATIONAL RESOURCES ON REGENERATIVE AND STEM CELL THERAPY PRACTICES

[The Australian Stem Cell Handbook 2015](#)

[Stem Cell Basics \(National Institutes of Health\)](#)

[Stem Cell Patient booklet \(Albany Medical College\)](#)

[A closer look at Stem Cells \(International Society for Stem Cell Research\)](#)

[Patient Handbook on Stem Cell Therapies \(International Society for Stem Cell Research\)](#)

[Stem Cell Tourism \(California Institute for Regenerative Medicine\)](#)

[The Power of Stem Cells \(California Institute for Regenerative Medicine\)](#)

[SCOPE: Learn About Stem Cells in Your Native Language \(The Niche\)](#)

LAMAR ALEXANDER
TENNESSEE

United States Senate

WASHINGTON, DC 20510

April 21, 2017

Gregory B. Snyder, MD, DABR
Chair-Elect
Federation of State Medical Boards
1300 Connecticut Ave NW, Suite 500
Washington, DC 20036

Dear Dr. Snyder:

Doctors, researchers, and patients have identified regenerative medicine and adult stem cell therapies as potential treatments to heal damaged, diseased, or deteriorated tissues and organs. In recent years, some of that promise has been realized. There are new therapies to treat burn and skin wounds, diabetic ulcers, and damaged knee cartilage, and clinical trials are underway for currently untreatable diseases.^[1] Doug Oliver, a constituent of mine who was diagnosed with malattia leventinese, a rare form of macular degeneration, participated in a clinical trial that used his own adult bone marrow stem cells to restore his eyesight.^[2] His remarkable progress is a testament to the potential of these treatments, and one of the reasons it was so important to pass the 21st Century Cures Act to provide clarity for regenerative medicine regulated by the Food and Drug Administration.

Unfortunately, recent reports indicate that some patients have been harmed by unproven or investigational treatments received at stem cell clinics. In one evaluation, published in *The New England Journal of Medicine*, three patients developed severe bilateral vision loss as a result of an injection of adult adipose tissue-derived stem cells.^[3] Other reports find stem clinics advertising their therapies as having the potential to treat diseases like Parkinson's or multiple sclerosis, including in circumstances where little, if any, evidence of their efficacy exists.^[4] Therefore, I urge your organization to develop best practices for state medical and osteopathic regulatory boards to follow regarding promotion, communication, and practices at stem cell clinics. I also seek information on the following questions:

1. How do state medical boards investigate complaints against stem cell clinics?
2. How are the existing false claims best practices enforced or used by state medical boards?
3. Are there standards or best practices regarding the use and communication of novel technology, such as adult stem cells?

^[1] <https://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=62>

^[2] <http://www.tennessean.com/story/opinion/contributors/2016/06/19/restored-sight-shows-potential-stem-cell-therapy/86042514/>

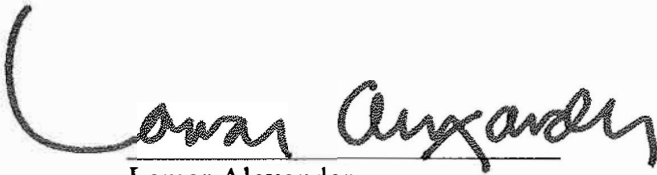
^[3] <http://www.nejm.org/doi/full/10.1056/NEJMoa1609583>

^[4] <https://www.nytimes.com/2016/07/28/upshot/stem-cell-therapies-are-still-mostly-theory-yet-clinics-are-flourishing.html>

3. Are there standards or best practices regarding the use and communication of novel technology, such as adult stem cells?
4. Are there standards for education necessary before implementing novel technology, such as adult stem cell procedures?

Thank you.

Sincerely,

A handwritten signature in black ink that reads "Lamar Alexander". The signature is written in a cursive style with a large, sweeping initial "L".

Lamar Alexander
U.S. Senator