Compliance Considerations for Entities Providing Hybrid Clinical Trial Services

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Introduction

COVID-19 disrupted a plethora of clinical trials. With social distancing measures firmly in place and many institutions only seeing patients for urgent needs, clinical trials were stalled indefinitely, which means investigative treatments were also stalled. COVID-19 also spurred, and in many ways forced, unprecedented use of telehealth. Not surprisingly, institutions began implementing telehealth into clinical trials. Since the beginning of COVID-19, clinical trials have been leveraging the powerful tool of telehealth, which promises to effectively blow the doors off of the geographic barriers that have long plagued clinical trial enrollment. A somewhat newly minted business model has emerged—hybrid clinical trial services. Here, an entity supports a clinical trial by providing clinicians that can carry out elements of a protocol *via* telehealth and elements of a clinical trial *via* in home services. The study subject may never have to enter an investigator's brick and mortar office. Entrants into this burgeoning field and industry sponsors are inquiring about how to structure this offering compliantly and how to utilize telehealth compliantly.

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Clinical Research as the Practice of Medicine

Companies interested in providing hybrid clinical trial services have a threshold issue to resolve; is carrying out the clinical aspects of a clinical trial the practice of medicine? Some argue that simply carrying out the clinical aspects of a predetermined protocol is not the practice of medicine. Others point to the clinical care required in the context of an adverse event, which requires independent clinical judgement on the part of the clinician.

There exists evidence under state law that performance of clinical research constitutes the practice of medicine. Under Tex. Admin. Code § 177.1(2)(emphasis added), Texas defines actively engaged in the practice of medicine as follows:

> The physician on a full-time basis is engaged in diagnosing, treating or offering to treat any mental or physical disease or disorder or any physical deformity or injury or performing such actions with respect to individual patients for compensation and *shall include clinical medical research, the practice of clinical investigative medicine*, the supervision and training of medical students or residents in a teaching facility or program approved by the Liaison Committee on Medical Education of the American Medical Association, the American Osteopathic Association or the Accreditation Council for Graduate Medical Education, and professional managerial, administrative, or supervisory activities related to the practice of medicine or the delivery of health care services. The term 'full-time basis,' for purposes of this section, shall mean at least 20 hours per week for 40 weeks duration during a given year.

Texas, therefore, explicitly includes "*clinical medical research*" in its definition of the practice of medicine, as well as "professional managerial, administrative, or supervisory activities related to the practice of medicine or the delivery of health care services." Not all states will necessarily agree with Texas, but the fact that there exists states such as Texas that explicitly include clinical medical research in the definition of engaging in the practice of medicine means that entities entering the clinical research support services space must consider this issue when thinking about building a scalable corporate structure.

Corporate Practice of Medicine

If, in a given state, practicing clinical research constitutes the practice of medicine, the corporate practice of medicine doctrine must be considered. Under this doctrine, a number of states prohibit the practice of licensed professions by general corporations, and, instead, require that licensed professions operate *via* a professional corporation or association. In the context of clinical trials, the corporate practice of medicine doctrine prohibits an entity from delivering medical services or employing physicians if the entity is owned by lay persons (*i.e.*, non-physicians).

The theory underlying the corporate practice of medicine is that clinicians, by virtue of, for example, having taken the Hippocratic Oath, must make decisions based on what is in the best interest of a patient, whereas officers and employees of general corporations must make decisions based on profit maximizing principles. The underlying incentives for non-licensed professionals could result in decision-making that is not in the best interest of a patient. This is a state law issue, and some states have no prohibition on the corporate practice of medicine. Nonetheless, many states have enacted corporate practice laws and regulations that prohibit this scenario from ever occurring by limiting ownership in professional corporations or associations to licensed clinicians.

For example, through statutes, regulations, court opinions, and medical board opinions, the law in Texas prohibits general corporations from practicing medicine, or employing or contracting with physicians to practice through such entities, because such entities cannot hold a medical license.[1] Under Tex. Admin. Code § 177.17(a), Texas law "generally prohibits corporations, entities or non-physicians from practicing medicine." Tex. Occ. Code § 155.001 restricts any person from practicing medicine unless the person is a licensed physician. Further, Tex. Occ. Code § 165.156 states that a "person, partnership, trust, association, or corporation commits an offense if the person, partnership, trust, association, or corporation, through the use of any letters,

words, or terms affixed on stationery or on advertisements, or in any other manner," indicates that such person, corporation, or other entity is entitled to practice medicine if such person or entity is not licensed to do so.[2]

Arizona case law generally prohibits corporations and other non-professional business entities from employing health care practitioners to render professional services.[3] Arizona Title 32, ch. 13, Art. 1 defines a "Doctor of Medicine" as a "natural person holding a license, registration or permit to practice medicine pursuant to this chapter."[4]

Colorado prohibits the practice of medicine by non-professional corporations and prohibit licensed professionals from accepting employment from unlicensed person. Colo. Rev. Stat. Ann. § 12-36-134(7) provides, "(a) Corporations shall not practice medicine. Nothing in this section shall be construed to abrogate a cause of action against a professional corporation for its independent acts of negligence. (b) Employment of a physician in accordance with section 25-3-103.7, C.R.S., [addressing hospitals] shall not be considered the corporate practice of medicine.". There is additional guidance on this issue in the context of a dental practice. Colorado defines it as unprofessional conduct to practice medicine as the partner, agent, or employee of, or in joint venture with, any person who does not hold a license to practice within the state.[5]

Friendly-PC Model

Entities with lay ownership interested in entering into the clinical trial business must consider compliance with the corporate practice of medicine where such laws exist. Many such entities opt to adopt a friendly-PC structure, which is a professional corporation (PC) organized for the purpose of conducting a medical practice in affiliation with a management services organization (MSO). This structure is designed to comply with state corporate practice of medicine restrictions that would prevent a non-professional or a business corporation from practicing medicine or related professions. This is an attractive option for entities founded by non-physicians or that plan to seek external capital funding resulting in lay ownership (*i.e.*, ownership by non-physicians). The affiliation between the MSO and the friendly PC is achieved through a hand-in-hand close working relationship between the MSO and the PC owner, as well as a series of contractual agreements, the MSO's provision of management services, and sometimes start-up financing for the PC. The overall arrangement is intended to allow the MSO to handle the management side of the PC's operations without infringing on the professional judgment of the PC or the medical practice of its physicians and the PC owner.

If structured and *operationalized* properly, the friendly PC model is intended to withstand allegations that the management company or its owners are violating the prohibition on corporate practice of medicine. Notwithstanding the foregoing, the friendly PC model is not "bulletproof" and there remains an irreducible risk it may be challenged as disallowed, particularly in states with a history of strong enforcement of the prohibition on the corporate practice of medicine. Despite the regulatory risk, companies use a friendly PC structure, and the structure generally remains the best-available model for achieving the business goals of the lay owners of a management company. The regulatory risks have historically been accepted by lay owners and investors, many of whom use some form of friendly PC model in states with corporate practice of medicine restrictions.

PC Owner

In addition to corporate practice considerations, a number of states require that a professional corporation owner be licensed to practice in the state in which the entity is operating. For example,

Utah law provides, "Except as provided in Subsection (1)(b), a person may not be an officer, director, or shareholder of a professional corporation unless that person is: (i) an individual licensed to render the same specific professional services as those for which the corporation is organized; or (ii) qualified to be an officer, director, or shareholder under the applicable licensing act for the profession for which the corporation is organized." "A professional corporation may issue the shares of its capital stock and a shareholder may voluntarily transfer shares of capital stock in a professional corporation only to: (a) persons who are duly licensed to render the same specific professional services as those for which the corporation was organized; or (b) persons other than those meeting the requirements of Subsection (1)(a) to the extent and in the proportions allowed by the applicable licensing act for the profession for which the corporation is organized."[6] "Professional service" means "the personal service rendered by: (a) a physician, surgeon, or doctor of medicine holding a license under Title 58, Chapter 67, Utah Medical Practice Act, and any subsequent laws regulating the practice of medicine."[7]

Similarly, Colorado law provides, "Except as specified in subparagraph (II) of this paragraph (d), all shareholders of the corporation are persons licensed by the board to practice medicine in the state of Colorado who at all times own their shares in their own right; except that one or more persons licensed by the board as a physician assistant may be a shareholder of the corporation as long as the physician shareholders maintain majority ownership of the corporation."[8]

The result of these state imposed licensure requirements is that entities interested in forming a friendly-PC must also identify and contract with a physician owner of the applicable professional corporation or association that is appropriately licensed in each such state.

Investigator Licensure

In addition to the friendly-PC owner requiring licensure in a number of states, the clinicians providing clinical services generally must be licensed in the state in which the study subject is located. This is an important principle in the context of hybrid clinical trials. While most appreciate that a clinician providing in home clinical care generally must be licensed in the state in which the study subject is located, but it is less clear whether the principal investigator or sub-investigator must be so licensed.

An investigator of a U.S. Food & Drug Administration (FDA) regulated clinical trial, means, in the context of a drug of biological clinical trial, an individual who actually conducts a clinical investigation (*i.e.*, under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Subinvestigator" includes any other individual member of that team.[9] In the context of a medical device clinical trial, an investigator an individual who actually conducts a clinical investigation, that is, under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.[10] In either case, the investigator has primary responsibility for the administration of the investigational product and ultimately conduct of the clinical trial.

FDA explains in the applicable guidance that when conducting clinical trials for which drugs, including biological products, under 21 CFR § 312 and of medical devices under 21 CFR § 812, are being investigated, an investigator is responsible for:

- Ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical

investigations of drugs, including biological products, or agreement for clinical investigations of medical devices, the investigational plan, and applicable regulations;
- *Protecting the rights, safety, and welfare of subjects under the investigator's care*; and
- Controlling drugs, biological products, and devices under investigation.[11]

As part of protecting the rights, safety, and welfare of a study subject under the investigator's care, investigators are expected to:
- Provide reasonable medical care for study subjects for medical problems arising during participation in the trial that are, or could be, related to the study intervention;
- Provide reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (*e.g.*, when the investigator is unavailable, when specialized care is needed); and
- Adhere to the protocol so that study subjects are not exposed to unreasonable risks.[12]

The responsibilities of an investigator clearly contemplate providing clinical care outside the context of a specific protocol, which necessarily includes exercising clinical decision-making—a hallmark of medical practice. FDA has noted, "During a subject's participation in a trial, the investigator (or designated subinvestigator) should ensure that reasonable medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial participation."[13] Providing clinical care to a study subject by an investigator, therefore, logically requires that the investigator be licensed in the state in which the study subject is located (even if the clinical services are being provided *via* telehealth).

Delegation of Clinical Duties

Investigators routinely delegate specific duties required under an applicable protocol. Nonetheless, when tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated.[14] While FDA assesses the adequacy of supervision by an investigator by probing: (1) whether individuals who were delegated tasks were qualified to perform such tasks, (2) whether study staff received adequate training on how to conduct the delegated tasks and were provided with an adequate understanding of the study, (3) whether there was adequate supervision and involvement in the ongoing conduct of the study, and (4) whether there was adequate supervision or oversight of any third parties involved in the conduct of a study to the extent such supervision or oversight was reasonably possible,[15] state licensure boards on the other hand, concern themselves with whether the clinical procedures performed are within the clinicians scope of practice and, if applicable, the existence and sufficiency of a collaborative practice agreement.

If, for example, a physician assistant (PA) is providing in-home clinical trial related services to a study subject located in Alabama, the PA and the physician would be required to possess licenses to provide clinical care by their respective Alabama licensure boards. Moreover, Alabama provides, "There shall be no independent unsupervised practice by an assistant to physician who is granted a license to practice as an assistant to physician."[16] The qualifications for a supervising physician are set forth in the Board's rules and require, among other things, that the physician be licensed in the State of Alabama and be regularly engaged in the full-time practice of medicine.[17] If the "physician [is] not regularly engaged in the full-time practice of medicine and/or in the circumstance where the physician and the physician assistant seeking registration are each employees of a legal entity other than a professional partnership, medical professional corporation, medical

professional association or physician practice foundation" the PA must demonstrate to the Board that the requisite supervisory relationship exists between the proposed supervising physician and the PA based on a series of factors set forth in the Board's rules.[18] Under Alabama law, "physician supervision" is defined, in relevant part, to mean "[a] formal relationship between a licensed assistant to a physician and a licensed physician under which the assistant to the physician is authorized to practice as evidenced by a written job description approved in accordance with this article."[19] Under the Board's rules, the job description must be signed by both the PA and the supervising physician, submitted with the PA's completed application for registration.[20]

Not only must supervisory requirements be met, if applicable, in the state in which a study subject is located, but a number of states explicitly address whether such supervision may be provided remotely. In Alabama, for example, the supervising physician is not required to provide direct on-site supervision of the PA; however, the supervising physician must provide the professional oversight and direction required by the Board's rules and guidelines, and the requirements must be outlined in the registration agreement if the PA is practicing off-site.[21]

Telehealth Practice Standards

In addition to licensure and supervisory requirements, clinicians providing clinical services in the context of a clinical trial must abide by the applicable state's telehealth practice standards. Clinicians must comply with the modality requirements of the state in which the study subject is located, for example. In Maine, "telemedicine," is defined by the medical board, means the practice of medicine or the rendering of health care services using electronic audio–visual communications and information technologies or other means, including interactive audio with asynchronous store-and-forward transmission, between a licensee in one location and a patient in another location with or without an intervening health care provider. Telemedicine includes asynchronous store-and-forward technologies, remote monitoring, and real-time interactive services, including teleradiology and telepathology. Telemedicine shall not include the provision of medical services only through an audio-only telephone, e-mail, instant messaging, facsimile transmission, or U.S. mail or other parcel service, or any combination thereof.[22] Similarly, the Kansas Telemedicine Act, defines "telemedicine," including "telehealth," to mean the delivery of healthcare services or consultations while the patient is at an originating site and the healthcare provider is at a distant site. Telemedicine shall be provided by means of real-time two-way interactive audio, visual, or audio–visual communications, including the application of secure video conferencing or store-and-forward technology to provide or support healthcare delivery, that facilitate the assessment, diagnosis, consultation, treatment, education, and care management of a patient's healthcare. "Telemedicine" does not include communication between:

(A) Healthcare providers that consist solely of a telephone voice-only conversation, email or facsimile transmission; or

(B) a physician and a patient that consists solely of an email or facsimile transmission.[23]

In addition to modality considerations, clinicians must abide by any state-specific disclosure and identity confirmation requirements. For example, The Kansas State Board of Healing Arts addresses patient identify verification by requiring that a licensee using telemedicine in the provision of healthcare services to a patient (whether existing or new) take appropriate steps to establish and maintain the licensee–patient relationship. The Board stresses the importance of each licensee using telemedicine to verify the

identity and location of the patient, and, provide the licensee's name, location, and professional credentials to the patient. Licensees prescribing medication, including controlled substances, by means of telemedicine are expected to comply with all state and federal laws, including licensure. When prescriptions *via* telemedicine are permissible, the licensee should implement measures to uphold patient safety in the absence of traditional physical examination. Such measures should guarantee that the identity of the patient and provider are clearly established and there is detailed documentation for the clinical evaluation and resulting prescription. Measures to assure informed, accurate, and error prevention prescribing practices are encouraged.[24]

In Maryland, for example, applicable regulations require that a telehealth practitioner shall develop and follow a procedure to verify the identification of the patient receiving telehealth services.[25]

The majority of states do not state *how* to accomplish patient identification, but require reasonable mechanisms.

Telehealth Informed Consent

In addition to the standard informed consent requirements applicable to clinical trials,[26] a number of states have specific telehealth informed consent requirements. For example, Cal. Bus. & Prof. Code § 2290.5 provides:

> (b) Prior to the delivery of health care via telehealth, the health care provider initiating the use of telehealth shall inform the patient about the use of telehealth and obtain verbal or written consent from the patient for the use of telehealth as an acceptable mode of delivering health care services and public health. The consent shall be documented.
>
> (c) Nothing in this section shall preclude a patient from receiving in-person health care delivery services during a specified course of health care and treatment after agreeing to receive services via telehealth.

Entities utilizing telehealth are well advised to review and institute applicable telehealth consent requirements in addition to the standard informed consent required for clinical trials.

Conclusion

Although several companies have emerged that provide clinical trial services and leverage telehealth in addition to providing in-home clinical services, a host of compliance considerations must be addressed for such entities to enter the market without undertaking substantial risk. Corporate structure and telehealth practice standards must be reviewed, understood, and implemented if the hybrid clinical trial model will sustain a compliance audit and survive in the long run.

Endnotes

1. *See* Tex. Occ. Code § 165.156 (making it unlawful for any individual, partnership, trust, association or corporation by use of any letters, words, or terms, as an affix on stationery or advertisements or in any other manner, to indicate the individual, partnership, trust, association or corporation is entitled to practice medicine if the individual or entity is not licensed to do so).
2. While Texas's corporate practice of medicine rule (Tex. Admin. Code § 177.17) provides for explicit exceptions to the prohibition under subsection (b), these explicit exceptions are limited to hospitals, the federal government, the military, private non-profit medical schools, school districts, state institutions, and rural health clinics, as well as specified Hospital Districts within the State of Texas.
3. *See Midtown Medical Group, Inc., v. State Farm Mutual Auto Insurance Co.*, 220 Ariz. 341 (Ariz. Ct. App. 2008).
4. *See* Ariz. Rev. Stat. Ann. § 32-1401.
5. Colo. Rev. Stat. Ann. § 12-36-117(m).
6. Utah Code Ann. § 16-11-8(1)(a); see also Utah Code Ann. § 16-11-7.
7. Utah Code Ann. § 16-11-2(3)(a).
8. *See* Colo. Rev. Stat. Ann. § 12-36-134.
9. *See* 21 CFR § 312.3(b).
10. *See* 21 CFR § 812.3(i).
11. *See* 21 CFR § 312.60; 21 CFR § 812.100; FDA, Guidance for Industry Investigator Responsibilities—Protecting the Rights, Safety, and Welfare of Study Subjects (Oct. 2009), *https://www.fda.gov/media/77765/download*.
12. FDA, Guidance for Industry Investigator Responsibilities—Protecting the Rights, Safety, and

Welfare of Study Subjects (Oct. 2009), *https://www.fda.gov/media/77765/download*.

13. *Id*.
14. *Id*.
15. *Id*.
16. Ala. Code § 34-24-295.
17. Ala. Admin. Code R. 540-X-7-.17 (Qualifications of The Supervising Physician--Physician Assistants (P.A.)).
18. See Ala. Admin. Code R. 540-X-7-.22 (Physician Assistants (P.A.) Not Employed By Supervising Physician/Physician Not In Full-Time Practice).
19. Ala. Code § 34-24-290(6); *see* Ala. Admin. Code R. 540-X-7-.01(10) (regulation containing similar definition of "physician supervision" to the statute).
20. Ala. Admin. Code R. 540-X-7-.15(3).
21. Ala. Code § 34-24-290(6); Ala. Admin. Code R. 540-X-7-.01(10).
22. Maine Department of Professional and Financial Regulation, Board of Licensure in Medicine, Telemedicine Standards of Practice, *https://www.maine.gov/md/sites/maine.gov.md/files/inline-files/Chapter_6_Telemedicine%20.pdf*.
23. *See* K.S.A. § 40-2,211(a)(5).
24. K.S. Bd. Healing Arts, Telemedicine.
25. Md. Code Regs. 10.32.05.04.
26. *See* 21 CFR part 50.