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Darshan Kulkarni, Esq.
The Kulkarni Law Firm
1657 The Fairway #1344
Jenkintown, PA 19046
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To: Whom It May Concern

Subject: Flexibility associated with compensation for services rendered in the context of clinical research conducted at clinical trial sites

Introduction

The Site Council has requested that we summarize the flexibility associated with study sponsor compensation for clinical study services provided by or on behalf of physicians conducted at clinical research sites. While a variety of business, legal and compliance issues are relevant to this question, a central issue is the valuation of the services at fair market value and the applicability of the federal anti-kickback law.

Definition of Fair Market Value

The Centers for Medicare and Medicaid Services ("CMS") previously defined fair market value ("FMV") as "the value in arm's-length transactions, consistent with the general market value." CMS has since clarified that instead of simply fair market value as a single definition applicable to all situations, it is more appropriate to consider separate definitions for general services, equipment rental, and office space rental, depending on the arrangement being considered. FMV for physician services is generally defined as: "The value in an arm's-length transaction, consistent with the general market value ("GMV") of the subject transaction."[1]

Similar changes were made to the definitions for general market value ("GMV") to differentiate between the general market value of compensation, assets, or the rental of equipment or office space. General market value of compensation for services is now defined as: "the compensation that would be paid at the time the parties enter into the service arrangement as the result of *bona fide* bargaining between well-informed parties that are not otherwise in a position to generate business for each other." [2]

[1] 42 CFR 411.351
[2] 42 CFR 411.351

Federal Anti-Kickback Summary

The Federal anti-kickback statute makes it a criminal offense to knowingly and willfully offer, pay, solicit, or receive any remuneration to induce, or in return for, the referral of an individual to a person for the furnishing of, or arranging for the furnishing of, any item or service reimbursable under a Federal health care program.[3] For purposes of the Federal anti-kickback statute, "remuneration" includes the transfer of anything of value, directly or indirectly, overtly or covertly, in cash or in kind. The statute has been interpreted to cover any arrangement where one purpose of the remuneration is to induce referrals for items or services reimbursable by a Federal health care program.[4]

Pharmaceutical companies and other purchasers of clinical research services have valid concerns that CMS may interpret higher than standard compensation to a clinical research facility ("Site") as an illegal kickback to induce the physicians at that Site to prescribe the company's products. Any such higher pricing must, therefore, be justified based on FMV and related principles.

FMV Does Not Mean Paying Every Site the Same Rates

As previously stated, compensation for services should be based on "compensation that would be paid at the time the parties enter into the service arrangement as the result of *bona fide* bargaining between well-informed parties that are not otherwise in a position to generate business for each other."[5]

The price charged for services offered may vary from Site to Site and will depend on a variety of factors, including, but not limited to, supply and demand of the clinicians and teams in question, accreditation requirements, reputation, skills and knowledge base of the clinicians in question, administrative duties, responsibilities and documentation required[6], the complexity of the research study (hereinafter "Study"), the timelines associated with the Study, the location of the Site, the cost of operating the Site and/or Study in that location, the cost of temporary and/or permanent resources required, and the Site's cost of capital. Some of these factors and others are often categorized as "Overhead." Overhead costs and rates vary from Site to Site. A "well-informed"[7] company taking responsibility for and initiating a clinical investigation (hereinafter "Sponsor") knows that large academic and healthcare institutions generally have significantly higher overhead as compared to small outpatient clinics. Some large

[3] 42 U.S.C. § 1320a-7b(b)

[4] E.g., United States v. Nagelvoort, 856 F.3d 1117 (7th Cir. 2017); United States v. McClatchey, 217 F.3d 823 (10th Cir. 2000); United States v. Davis, 132 F.3d 1092 (5th Cir. 1998); United States v. Kats, 871 F.2d 105 (9th Cir. 1989); United States v. Greber, 760 F.2d 68 (3d Cir. 1985).

[5] 42 CFR 411.351

[6] *See* Determination of the Fair Market Value of Oncology Advanced Practitioners, J Adv Pract Oncol 2020;11(2):191–195

[7] 42 CFR 411.351

academic institutions have standard overhead rates exceeding 50 percent. Such a standard overhead rate would be unusual for smaller Sites.

In light of the various factors influencing Sponsor requirements, market conditions, and the Overhead and related reasonable charges associated with the services, a Sponsor engaged in a "bona fide [bargain]"[8] with a Site is unlikely to pay the same rate for every service at every Site or possibly even across departments at the same institution. Accordingly, paying all the Sites the same rate despite a variety of factors influencing pricing decisions may not comport with GMV principles and may result in violations of the federal Anti-Kickback law.

Whatever the bargain struck between a Sponsor and a Site for a specific Study, the pricing must be justifiable by both sides to CMS based on the Site's costs, the reasonable charges delivered to the Sponsor, the value the market places on the Site's participation, and other factors. While reasonable variations in pricing can be within the bounds of normal FMV, the justification for larger variations should be documented.

Clinical Research Pricing vs. Regular Clinical Pricing

To avoid triggering the federal anti-kickback law by paying more than FMV, some Sponsors insist they will pay Sites only the equivalent of, or a multiple of, reimbursement provided by government or private third-party payors for services rendered as part of the standard of care. This reimbursement strategy, though routinely used, has its limitations. Unlike services rendered in the course of providing the standard of care, services rendered in the course of clinical research generally involve additional costs including, but not limited to, the cost of executing non-standard-of-care procedures and assessments, the cost of additional documentation, the cost of additional training, the cost of additional technology, the cost of additional administration to manage the Study, and the cost of additional liability insurance. Additionally, standard of care is generally not subject to the additional costs incurred to demonstrate compliance with FDA requirements to internal auditors, institutional review boards, Sponsors and contract research organizations. Additionally, while payment by governmental and other third-party payors can generally be relied upon, payment by Sponsors, especially smaller ones, entails a higher risk. When a Site contracts to conduct a Study, there may be great uncertainty in the number of patients it will enroll In the Study and the actual costs associated with conducting the Study. Accordingly, the additional efforts, costs and risks taken before, during and after the services are rendered may reasonably result in different prices for clinical services versus clinical research services.

Conclusion

In summary, determining FMV pricing in the context of clinical research is nuanced and multifaceted. Accordingly, a one-size-fits-all approach is unlikely to apply in all circumstances. Furthermore, the

[8] 42 CFR 411.351

variability in payment between clinical practice and research, for what may appear to be the same services, underscores the importance of a well-considered, individualized approach to setting prices consistent with FMV.

Limitations

This summary analysis is intended to be a general summary discussion and has the following limitations applicable to this summary analysis:

1. This summary analysis is issued only to the Site Council, the requestor of this opinion. This summary analysis has no application to, and cannot be relied upon by, any other individual or entity.
2. This summary analysis is not intended and should not be used to be introduced into evidence by any person or entity.
3. This summary analysis is applicable only to the statutory provisions specifically noted above. No opinion is expressed or implied herein with respect to the application of any other Federal, state, or local statute, rule, regulation, ordinance, or other law that may be applicable, including, without limitation, the Physician Self-Referral Law, section 1877 of the Act (or that provision's application to the Medicaid program at section 1903(s) of the Act), the Federal Exclusion Statute, the Civil Monetary Penalties Law, the False Claims Act, state and local laws.
4. This summary analysis will not bind or obligate any of the signatories to this summary analysis.
5. This summary analysis is limited in scope to the general, limited, summary analysis described above, and has no applicability to any individual assessment or other arrangements, even those of which general analysis appear similar in nature or scope.