

Personalized Medicine Molecular Genetic Laboratory Testing Legal Compliance Traps

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I. Introduction

Laboratory testing is one of the primary tools physicians have to gather diagnostic information for use in treating patients. Personalized medicine, including molecular genetic testing, presents the possibility of improved medical decision-making. It can provide information about the predictive risks of a disease, as well as information that may be helpful in choosing among treatment alternatives. “The concept of ‘personalized medicine’ has evolved to incorporate personal genomic information into a patient’s clinical assessment and family history to guide medical management.”¹ At the heart of personalized medicine is the goal of tailoring patient care in light of the molecular basis for a disease and the individual patient’s likely response to a specific treatment.

Numerous legal barriers may limit realizing the enormous promise of personalized medicine. This article discusses the following compliance implications faced by laboratories advancing personalized medicine through molecular and genomic testing:

- Molecular laboratory licensure and regulatory requirements;
- Reimbursement challenges for new molecular testing;
- Medicare coding and billing requirements; and
- Compliance guidelines for molecular laboratory collaborations and customer relationships.

A. Molecular Laboratory Licensure/Regulatory Requirements

The safety and quality of medical laboratory testing are regulated by multiple government agencies in various ways, including state licensing, federal quality standards, and restrictions on the use and marketing of medical devices. The following is a brief description of the regulatory framework applicable to a molecular laboratory.

1. The Food & Drug Administration

The Food & Drug Administration (“FDA”) regulates the safety and efficacy of medical devices. Molecular tests are medical devices regulated by FDA.² FDA has issued regulations for medical services that address adulteration; misbranding; device registration and listing; premarket notification; banned devices; notification, including repair, replacement, or refund; records and reports; restricted devices; and good manufacturing practices.

A “device” is defined under the Food, Drug and Cosmetic Act (“FDCA”) to include an article “intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals. . . .”³ FDA classifies medical devices as Class I, II, or III,

according to the level of regulatory control that FDA deems necessary to provide a reasonable assurance of safety and effectiveness.⁴

Genomic and molecular laboratories often develop their own lab tests, referred to as home brew tests, in-house tests, or laboratory developed tests (referenced here as “LDTs.”). LDTs frequently use generally available testing reagents and equipment. LDTs are defined by FDA as tests developed “by a single clinical laboratory for use only in that laboratory.”⁵ The reliance on generally available reagents and general purpose equipment has been a key factor influencing FDA’s regulatory approach:

[C]linical laboratories that develop [in-house] tests are acting as manufacturers of medical devices and are subject to FDA jurisdiction under the Act . . . [however, FDA] has generally [chosen to] exercise . . . enforcement discretion over standard lab-developed tests that use primarily analyte specific reagents, general purpose reagents, general purpose laboratory equipment, other laboratory instrumentation, and controls.⁶

Analyte specific reagents (“ASRs”) are defined by federal regulation as:

[A]ntibodies, both polyclonal and monoclonal, specific receptor proteins, ligands, nucleic acid sequences, and similar reagents which, through specific binding or chemical reactions with substances in a specimen, are intended for use in a diagnostic application for identification and quantification of an individual chemical substance or ligand in biological specimens.⁷

FDA has determined that ASRs are medical devices subject to its regulations.⁸ Thus, the companies that manufacture the reagents and equipment used in LDTs are subject to customary FDA regulation as well as certain FDA standards which impact the manufacturer’s marketing.

FDA elected to exercise discretion and not subject LDTs to pre- or post-market approval, relying instead on its regulation of the reagents and equipment

used in LDTs, because FDA “believed it was regulating the primary ingredients of most in-house developed tests, and because it believed that laboratories certified as high complexity under [CLIA] . . . have demonstrated expertise and ability to use ASRs in test procedures and analyses.”⁹

However, in 2006, when FDA issued the *Draft IVDMIA Guidance*, it revisited its 1997 guidance and expressed concern that when in vitro diagnostic multivariate index assays (“IVDMIA”) ¹⁰ rely on materials beyond ASRs and general purpose items, IVDMIAs should be subject to FDA regulation, while other LDTs should continue to be developed without pre- or post-market approval:

The FDA intends to issue guidance regarding those laboratory-developed tests over which it has in the past generally exercised, and over which it intends to continue to exercise, enforcement discretion. IVDMIAs must meet pre- and postmarket device requirements under the act and FDA regulations, including premarket review requirements in the case of class II and III devices.

This position was met with resistance by the laboratory industry, and the promised revised FDA-guidance has not yet been issued. Thus, for now, IVDMIAs are not subject to mandatory FDA pre- and post-market approval; the ASRs continue to be regulated.

FDA’s rules classify most ASRs as Class I devices, which therefore subjects these ASRs to the lowest level of FDA regulation. Consistent with the treatment of ASRs as building blocks for laboratory tests, the regulations generally prohibit ASR manufacturers from instructing the laboratory in developing or performing a test with the ASR. However, the manufacturer may provide to the laboratory information concerning proper storage, as well as

pertinent scientific data such as chemical/molecular composition, concentration or mass, nucleic acid sequence, binding affinity, cross-reactivities, known mutations associated with a sequence, and interaction with substances of known clinical significance.¹¹ However, FDA regulations provide that in the sale of ASRs within Class I, manufacturers may include only a general description concerning the quantity, proportion or concentration of the product and information about the manufacturer.

ASR manufacturers are further prohibited from making claims to physicians or laboratories regarding the analytical or clinical performance of their ASRs. Further, FDA regulations permit manufacturers to sell ASRs only to laboratories certified under CLIA to perform high complexity testing, discussed below; thus impacting how (and which) laboratories perform LDTs. FDA regulations also provide that only physicians or otherwise authorized persons may order tests which utilize ASRs. Further, FDA mandates that the laboratory using an ASR to perform an LDT must provide the following disclosure:

This test was developed and its performance characteristics determined by [Laboratory Name]. It has not been cleared or approved by the U.S. Food & Drug Administration.¹²

FDA has noted that some laboratories have used products or devices which lack FDA clearance and which can only be lawfully used for research or for investigational purposes, outside of the context of research or clinical investigations.¹³ To address this situation, FDA issued guidance which states the manufacturers should not sell “research use only” or “investigational use only” products to laboratories which they know will use the products for non-permitted

purposes, and the manufacturers should halt sales to those laboratories that they discover use the products for non-permitted purposes, or the manufacture should comply with FDA requirements for premarket review.¹⁴

As a consequence of FDA's election to exercise enforcement discretion, laboratories developing LDTs which use general purpose reagents and general purpose laboratory equipment currently enjoy significant freedom from FDA regulation; FDA has indicated that this will change. The universe of LDTs that will be regulated is uncertain. However, FDA indicates it will take a "risk-based application of oversight to LDTs".¹⁵ The proposed risk-based standards are not yet available.¹⁶ The guidance documents are currently under review within FDA and the date of release is not known at this time.

Molecular LDTs include in vitro diagnostic tests ("IVDs") and in vitro diagnostic multivariate index assays ("IVDMIA"). IVDMIA are generally more complex tests than IVDs. IVDs are defined as:

[R]eagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.¹⁷

Although FDA has yet to publish a final rule defining what constitutes an IVDMIA, FDA has proposed the following definition of an IVDMIA:

[A] device that (1) Combines the values of multiple variables using an interpretation function to yield a single, patient-specific result (e.g., a "classification," "score," "index," etc.), that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, and (2) Provides a result whose derivation is non-transparent and cannot be independently derived or verified by the end user.¹⁸

Over the past decade, LDTs have become more complex at an increasingly fast pace. FDA has assessed this state of affairs and determined to exercise more oversight of IVDMIAs:

IVDMIAAs raise significant issues of safety and effectiveness. These types of tests are developed based on observed correlations between multivariate data and clinical outcome, such that the clinical validity of the claims is not transparent to patients, laboratorians, and clinicians who order these tests. Additionally, IVDMIAs frequently have a high risk intended use. FDA is concerned that patients are relying upon IVDMIAs with high risk intended uses to make critical health care decisions when FDA has not ensured that the IVDMIA has been clinically validated and the health care practitioners are unable to clinically validate the test themselves. Therefore, there is a need for FDA to regulate these devices to ensure that the IVDMIA is safe and effective for its intended use.¹⁹

Although FDA has not finalized the regulatory system suggested in the Draft IVDMIA Guidance; it has completed pre-market review of certain IVDMIAs. The promised change to the regulation of IVDMIAs is a concern for the laboratory industry. If the currently proposed guidance were implemented, laboratories offering IVDMIAs would likely need to provide documented scientific support for any claims about clinical or analytical performance.

Some in the industry question whether such regulation is needed in light of other extensive regulatory processes which already apply to laboratories performing high complexity testing (including, the Clinical Laboratory Improvement Amendments of 1988 (“CLIA”),²⁰ the College of American Pathologists proficiency testing process, state licensing processes (such as the New York State Clinical Laboratory Evaluation Program that requires laboratories to document analytic and clinical validity prior to introducing a test), and various international proficiency testing agencies²¹).

2. Federal Quality Standards/CLIA License

The Centers for Medicare and Medicaid Services (“CMS”) has regulatory authority over laboratories pursuant to CLIA. CMS administers the CLIA laboratory certification program in conjunction with FDA and the Centers for Disease Control (“CDC”). FDA is responsible for test categorization, and CDC is responsible for CLIA studies, convening the Clinical Laboratory Improvement Advisory Committee (“CLIAC”), and providing scientific and technical support to CMS.

Regulations adopted under CLIA impose standards for proficiency testing,²² quality control requirements,²³ personnel requirements,²⁴ ongoing inspection,²⁵ and enforcement procedures.²⁶ Only laboratories in Washington and New York states are not required to secure CLIA certification; those states are exempt from CLIA on the basis of their rigorous pre-CLIA regulatory safeguards; as a result, their state laboratory quality standards preempt the CLIA standards.

CLIA defines a “laboratory” as:

[A] facility for the biological, microbiological, serological, chemical, immuno-hematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings.²⁷

Like any other clinical test, molecular tests are subject to all general CLIA rules. Since molecular tests are normally categorized as either moderate or high complexity tests, a laboratory performing molecular tests is required to apply for and obtain a [CLIA Certificate of Compliance or a Certificate of Accreditation]. . . Currently, there is no CLIA specialty or sub-specialty for molecular or biochemical genetic testing. Therefore, there are no special personnel, quality control, or proficiency-testing requirements for molecular tests, unless the laboratory voluntarily chooses

a CMS-approved accrediting organization specifying additional requirements.²⁸

The level of CLIA regulation applicable to a laboratory depends on the complexity level of approved tests which can be conducted in that laboratory. There are four levels of complexity: waived testing, provider-performed microscopy testing (select tests by physician/practitioners for their own patients), moderate complexity testing, and high complexity testing.²⁹

CLIA requires that a laboratory performing high complexity testing enroll in a CMS-approved proficiency testing program. When a test is not associated with a CLIA defined specialty, the laboratory is required to participate in an equivalent activity for such testing.³⁰ The regulations issued under CLIA do not include proficiency testing requirements that are specific to molecular genetic tests; therefore, laboratories providing molecular testing procedures may experience uncertainty in meeting this CLIA requirement.

CDC has provided the following guidance to laboratories that perform molecular genetic tests for which no proficiency testing program is available -

- Although no data are available to determine whether alternative performance assessments are as effective as proficiency testing, professional guidelines (e.g., from CLSI and CAP) provide information on acceptable alternative performance assessment approaches. [Internal citations omitted.] Laboratories that perform molecular genetic tests for which no proficiency testing program is available should adhere to these guidelines.
- Laboratories should ensure that alternative assessments reflect the test methods involved in performing the testing and that the number of samples in each assessment is adequate to verify the accuracy and reliability of test results.
- Ideally, alternative assessments should be performed through interlaboratory exchange or using externally derived materials, because

external quality assessments might detect errors or problems that would not be detected by an internal assessment. [Internal citations omitted.]

- When interlaboratory exchange or obtaining external materials is not practical (e.g., testing for rare diseases, testing performed by only one laboratory, patented testing, or unstable analytes such as RNA or enzymes), laboratories may consider options such as repeat testing of blinded samples, blind testing of materials with known values, exchange with either a research facility or a laboratory in another country, splitting samples with another instrument or method, or interlaboratory data comparison.³¹

3. States Also Regulate Laboratories

CLIA does not preempt state laws that provide more stringent regulation of laboratories than the CLIA rules. Accordingly, state laws may require additional personnel, qualifications, quality control, record maintenance, and/or proficiency testing that is mandated by CLIA. Further, applicable state laws may require a detailed review of the laboratory's scientific validations and technical procedures for tests before use or marketing of laboratory services. At least one state imposes specific additional requirements on laboratories performing molecular laboratory testing.³²

Several states require the pathologist working at a molecular laboratory to have a license if the physician routinely provides medical opinions for patients residing in the licensing state, even if the laboratory is located out of state.³³

B. Reimbursement Challenges for New Genomic Testing

1. Insurance Coverage of LDTs

Insurance coverage for novel molecular genetic LDTs varies across payors. Some payors have challenged coverage for an LDT under the theory that the utility of the test is unproven, and thus the test is not "reasonable and

necessary,” or has not been clinically proven to be useful in addressing a patient’s disease state. Further, reimbursement is complicated because coding and payment systems were not designed in a way that marries well with innovative health care services, such as LDTs that were not identified by their own unique CPT codes.

a. “Reasonable and Necessary” Requirements.

The insurance limitation of paying only for “reasonable and necessary” services is well grounded in the federal Medicare program:

Notwithstanding any other provision of this subchapter, no payment may be made . . . except for items and services [which] . . . are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member . . . [or] which are not reasonable and necessary for the prevention of illness.³⁴

FDA recognized in the Draft IVDMA Guidance that many LDTs lack clinical validation, thus setting the stage for denial of coverage due to the absence of proof that the tests will be useful in patient care.

Other private insurance companies rely on a “reasonable and necessary” standard (or something similar) in making their coverage decisions. Coverage often requires a showing that a molecular test has both clinical validity and clinical utility. Clinical validity refers to a test’s ability to detect or exclude a disease or condition in a patient as measured against designated criteria. Clinical utility refers to the usefulness of a test and the value of the information in medical decision making. In the absence of peer reviewed studies validating clinical utility, reimbursement for LDTs can be a challenge.

“One frequent tactic for establishing molecular test validity is the use of the case-control study. Case-control studies are studies in which a collection of

“cases” . . . and a collection of “controls” . . . are assembled and tested with the experimental diagnostic test.”³⁵ However, case-control studies have been criticized when used to evaluate test accuracy because studies often include “only unambiguous cases” and do not include difficult-to-diagnose cases.³⁶ With respect to clinical utility, a major challenge of molecular tests is the “lack of studies that directly correlate test results with clinical outcomes.”³⁷

“For most LDTs, data on analytical and clinical performance are not publicly accessible unless published in peer-reviewed journals. In contrast, FDA-approved or cleared commercially distributed test kits are accompanied by a kit insert that summarizes the analytical and clinical validity data submitted for approval; FDA Decision Summaries are publicly available via the FDA Web site.”³⁸ Because FDA does not specifically address clinical utility, clearance is not a direct path to coverage or payment.

b. Medicare Coverage Issues for LDTs.

Non-FDA-approved LDTs which meet CMS standards are approved through the CMS National Coverage Determination (“NCD”) or Local Coverage Determination (“LCD”) processes. Thus, Medicare has addressed the need to make coverage decisions concerning LDTs by allowing local level coverage determinations to be made by the Medicare Administrative Contractors (“MACs”). There are, and likely will continue to be, geographic disparities in coverage by Medicare of an LDT because each local MAC has the ability to determine whether coverage is appropriate in the absence of an NCD.

An example of the difficulty facing laboratories performing LDTs is illustrated by the issuance of an LCD by Palmetto GBA, a Medicare MAC, in October of 2011. (This LCD was later rescinded but was replaced with a substantially equivalent policy.) That LCD confirmed Palmetto’s adoption of a “no coverage” policy for any molecular diagnostic tests that are not explicitly covered by an NCD, LCD or coverage article published by Palmetto GBA.

2. Coding and Billing Challenges

Even if insurance coverage is available, laboratories struggle with billing and coding issues. The regulations implementing the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) adopted standards for the content and format of electronic health care transactions, including standards related to “code sets” and “transaction elements.” All health plans and health care providers are required to comply with these requirements.³⁹ HIPAA thus makes coding standards adopted by HHS “applicable to (1) all health plans, (2) all health care clearinghouses, and (3) any health care provider who transmits any health information in electronic form...”⁴⁰ The Current Procedure Terminology (“CPT”) Manual, published by the American Medical Association, lists HIPAA-compliant codes. Until 2012, many LDTs did not have a specific CPT code. Instead, molecular pathology services were billed using codes which identified the various procedures involved in performing each assay (e.g. CPT 83890 to 83914). Each code billed represented a separate step undertaken to complete the LDT. This is referred to as code stacking. Code stacking was useful to define the

methods used in performing an LDT, but did not provide information concerning what patient-medical condition was at issue.

The absence of information about why a test was being performed resulted in payor complaints that it was virtually impossible for them to know what tests they are actually paying for. It also resulted in laboratories which have developed comparable tests, but utilize different steps, to bill using widely-different codes; this resulted in dissimilar charges. Therefore, payors did not have comparability information for purposes of pricing tests which may be similar. In the absence of a clear understanding of what they were paying for, payors were limited in their ability to comparably price comparable services.

As an alternative approach to billing, some molecular laboratories approached the dual problems of correct coding and securing appropriate reimbursement by using miscellaneous CPT codes, referred to as not otherwise classified (“NOC”) codes. Often, the consequence of this approach was that every bill was subject to scrutiny. This additional scrutiny delayed ultimate reimbursement.

In light of these problems, in 2009 the AMA convened a panel (known as the CPT Molecular Pathology Coding Workgroup (the “Workgroup”)) charged with the task of constructing a new section in the CPT Manual to report molecular pathology services.

The Workgroup’s efforts led to the addition of a new Molecular Pathology section in the 2012 CPT Manual. This new section describes molecular pathology procedures. The codes listed in this new section are categorized in two groupings:

Tiers 1 and 2. The 2012 CPT Manual provides guidelines and definitions to clarify the use of the 101 new codes that were added as Tier 1 and 2 codes.

Tier 1 contains 92 codes (CPT Codes 81200 - 81383) which describe gene-specific and genomic procedures. For example CPT 81216 is defined by 2012 CPT as “BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis.” 2012 CPT describes CPT 82126 as defining the following procedure: “High quality DNA is isolated from whole blood and subjected to 47 individual PCR amplification reactions. The PCR products from each reaction undergo bidirectional dideoxynucleotide chain termination sequencing by capillary electrophoresis instrument. Sequence data analysis is performed by computer software, followed by visual inspection and confirmation under the direction of a certified laboratory director. Genetic variants are identified by comparison with a consensus wild-type reference sequence. A system-generated report is prepared that specifies the patient's mutation status to include information from an internal database and the literature regarding the significance of variants identified. The report is reviewed and signed by a pathologist or other health care provider. The results are communicated to the appropriate health care provider.” Thus, the code includes the test and the report.

Tier 2 contains nine codes (CPT Codes 81400-81408) which describe a molecular pathology procedure that is not listed in the Tier 1. CPT 2012 notes that the Tier 2 codes represent medically useful procedures that are generally performed in lower volumes than Tier 1 procedures (e.g., the incidence of the

disease being tested is rare). Tier 2 codes are arranged by the level of technical resources and interpretive work performed by the rendering professional.

If, when attempting to apply a Tier 2 code, the analyte tested is not listed, or is not represented by a Tier 1 code, the 2012 CPT instructs that we are to use the appropriate methodology codes in the CPT 83890-83914 range (i.e. codes intended for use with molecular diagnostic techniques for analysis of nucleic acids which are coded by procedure) or the CPT 88384-88386 series codes.

AMA also addresses the scope of services included in the new Tier 1 and Tier 2 codes. These new codes include all analytical services performed in the test (e.g., cell lysis, nucleic acid stabilization, extraction, digestion, amplification, and detection). However, the 2012 CPT Manual indicates that any procedures required prior to cell lysis (e.g., microdissection, codes 88380 and 88381) should be reported separately, and further, that all analyses are qualitative unless otherwise noted.

In addition, the AMA published new administrative codes for Multianalyte Assays with Algorithmic Analyses (“MAAAs”). These codes have **not** been reviewed by the AMA for clinical utility. These new codes will be first effective on September 15, 2012. MAAAs are defined by the AMA generally as laboratory- or manufacturer-specific tests that utilize multiple results derived from assays of various types, including molecular pathology assays, fluorescent in situ hybridization assays and non-nucleic acid based assays (e.g., proteins, polypeptides, lipids, carbohydrates) and require an algorithmic analysis in order to generate a result. Each MAAA code adopted by the AMA will have a 4 digit

identifier followed by the letter M. The format of the descriptor for these new MAAA CPT codes includes the following:

- Disease type (e.g., oncology, autoimmune, tissue rejection);
- Material(s) analyzed (e.g., DNA, RNA, protein, antibody);
- Number of markers (e.g., number of genes, number of proteins);
- Methodology(ies) (e.g., microarray, qRT-PCR, ISH, ELISA);
- Number of functional domains (if indicated);
- Specimen type (e.g., blood, fresh tissue, formalin-fixed paraffin embedded);
- Algorithm result type (e.g., prognostic, diagnostic); and
- Report (e.g., probability index, risk score).⁴¹

However, CMS did not include the resource value units for either the Tier 1 or Tier 2 codes or the MAAA codes in the 2012 Physician Fee Schedule; therefore, the new codes will not be valid for Medicare purposes for 2012. Instead, Medicare will continue to require the current “stacking” codes when billing for molecular pathology services. The requirement for listing as an MAAA code is commercial availability. Because CMS, at this time, will not assign a fee schedule value to any MAAA, Medicare reimbursement will be available only if the stacked codes on HOC codes have already been valued by the local contractor.

Whether CMS has the authority to refuse to recognize the HIPAA-compliant codes, is suspect. As stated earlier, all health plans and health care providers are required to comply with HIPAA requirements, including the requirement to use the designated code sets.⁴²

CMS has stated that each of the new AMA-adopted Molecular Pathology Codes “represents a test that is currently being used and which may be billed to Medicare. When these types of tests are billed to Medicare, CMS understands that existing Current Procedural Terminology (CPT) test codes are “stacked” to represent a given test. . . As of January 1, 2012, Medicare requests that Medicare claims for Molecular Pathology Procedures reflect both the existing CPT “stacked” test codes that are required for payment and the new single CPT test code that would be used for payment purposes if the new CPT test codes were active.”⁴³

C. Compliance Guidelines for Molecular Laboratory Collaborations and Customer Relationships

Although the expanding world of molecular lab testing will include existing life science companies (medical device and pharmaceutical manufacturers), as well as existing health care providers and laboratories, many new entrants will be companies from outside the health care industry.

As organizations with no prior experience in the lab world move into the business of performing and delivering molecular diagnostic testing, they and their legal counsel will be required to become familiar with the many regulatory limitations affecting commercialization of clinical laboratory testing, including those governing the business relationships between laboratories and other parties that are in a position to refer, or to influence the referral, of laboratory testing.

Medical device and pharmaceutical companies may have a working knowledge of the federal Medicare anti-kickback statute (“AKS”);⁴⁴ with its pertinent safe harbors, as applied to their industries. However, device and

pharmaceutical manufacturers may be less familiar with the federal physician self-referral law, better known as the “Stark law,”⁴⁵ and its key exceptions, because pharmaceutical products and medical devices do not constitute “designated health services” under the Stark law. In short, within the context of molecular lab testing, the Stark law prohibits a physician from referring Medicare patients to a molecular laboratory with which the physician has a "financial relationship" for the provision of lab testing and prohibits the molecular lab from billing for testing furnished pursuant to a prohibited referral, unless an exception applies. The Stark law is not an intent-based statute; thus, if a physician compensation arrangement does not meet a Stark law exception precisely, it is strictly prohibited.

1. Collaborative Business Models

As new and non-traditional players enter the molecular diagnostics marketplace, clinical laboratories, health systems, test manufacturers, pharmaceutical companies and contract research organizations have begun to forge new alliances.

Personalized medicine is a disruptive innovation that will require the development of new business models, particularly for health industry players....To compete in this market, organizations will need new approaches, new relationships, and new ways of thinking....As companies search for sustainable models, one theme has emerged clearly: the need for collaboration.⁴⁶

Parties considering and developing collaborative models between multiple separate entities to deliver molecular lab testing must understand and navigate current federal and state laws to determine the feasibility of particular models. This is of particular importance if the collaboration involves stakeholders that are

not fully integrated within a separate legal entity, and that are in a position to arrange for or recommend “purchasing, leasing or ordering any good, facility, service, or item for which payment may be made by in whole or in part under a Federal health care program.”⁴⁷ Our discussion focuses primarily on such models.⁴⁸

a. Shell Labs.

In particular, formation of so-called “shell labs” has been emphatically discouraged at the federal level. The term “shell lab rule” has been used differentially by regulators to describe two related yet distinct business practices involving laboratories — suspect joint ventures and pass-through billing. These federal “shell lab” rules may complicate the efforts of non-labs (including researchers or developers of important new molecular testing), to forge partnerships with existing labs to promote new molecular testing technology.

As early as 1989, in a Special Fraud Alert, OIG cautioned providers enrolled in federal programs to avoid “shell laboratory joint ventures,” in which a “shell” lab performs little if any testing, instead referring most testing to another laboratory, that may also serve as “manager” of the “shell” lab; yet the “shell” lab bills Medicare directly for all of the testing.⁴⁹ OIG has continued to express concerns about joint ventures involving little more than a “shell” with disproportionate business risk and responsibility allocation based upon one party’s ability to arrange or direct federal program referrals.⁵⁰

The other federal “shell lab” rule likewise limits the ability of a “shell” lab to bill for federal program testing the lab does not actually perform. Both

Medicare and Medicaid require direct billing by laboratories.⁵¹ Subject to limited exceptions, only the lab that actually performs the testing may bill Medicare. The rule also prohibits labs from assigning to anyone the right to claim Medicare reimbursement for testing performed by the lab. Moreover, as explained above, only a CLIA-certified may bill either Medicare or Medicaid. These direct billing rules effectively prevent non-lab entities, including pharmaceutical or device companies, from seeking or receiving federal program reimbursement for molecular lab testing, even if they are key players in developing and promoting the test.⁵²

The purpose and history of Medicare’s direct billing “shell lab” rule was explained in *Hanlester Network, et al., Melvin L. Huntsinger, M.D., Ned Welsh*:

The “shell lab” rule was contained in the Omnibus Budget Reconciliation Act of 1989...and limited the availability of reference laboratory billing to rural hospitals and other laboratories which send out no more than 30 percent of their tests....This limitation was intended to redress abuses of the reference laboratory billing exception, which had been intended to benefit small laboratories which had to send out certain “difficult or sophisticated tests,” by parties who had created laboratories that have only a limited capacity to do testing, or indeed have virtually no capacity to do testing, but that act as conduits for referrals to other laboratories.⁵³

Where no federal program reimbursement is involved, some states do not expressly prohibit reselling of lab testing, leaving open the possibility for a non-lab (perhaps as an interim step to building or buying its own lab) to purchase and resell lab testing to non-government payors, including private insurers, health care practitioners, and patients; subject to the CLIA requirement that labs may only accept orders from persons “authorized under state law to order tests or receive test results, or both.”⁵⁴ That option may be foreclosed by specific anti-assignment

provisions within payer contracts and policies, however. Likewise, re-billing arrangements may also be constrained by other states' laws limiting the resale of lab testing, through direct billing,⁵⁵ anti-markup,⁵⁶ and disclosure laws.⁵⁷

2. Contract Sales Models.

Occasionally, new lab participants are surprised to learn that marketing practices common in other commercial contexts may trigger Stark law and/or AKS restrictions. The AKS restrictions apply to a molecular lab's partnering contractually with a pharmaceutical or device manufacturer or other entity to leverage an existing customer base in order to promote molecular lab testing. The AKS also regulates programs to enlist health providers, especially referral sources, as conference presenters and panelists, consultants, or thought leaders; with additional Stark law requirements when the provider is a physician.

Both the AKS and the Stark law include exceptions for *bona fide* employees. The AKS statutory exemption for *bona fide* employees "permits an employer to pay the employee in whatever manner [it] chooses for having that employee assist in the solicitation of Medicare or State health care program business..."⁵⁸ Because the Stark law is directed at compensation arrangements with physicians who are themselves sources of federal program referrals, the Stark law exception for *bona fide* employment of physicians (to the extent allowed by state practice of medicine rules) is narrower than the AKS employment exemption, and would not permit percentage-based commissions

“determined in a manner that takes into account (directly or indirectly) the volume or value of any referrals by the employee.”⁵⁹

The AKS safe harbor for personal services,⁶⁰ however, is much more restrictive than the AKS employee exemption. Although OIG has stated specifically that “many advertising and marketing activities warrant safe harbor protection under the personal services and management contracts safe harbor,”⁶¹ OIG has expressed consistent disapproval of federal program providers’ paying contract sales personnel percentage-based sales commissions:

Commission-based compensation to contract sales force will not meet the personal services and management contracts safe harbor because it is ‘not fixed in advance and is determined in a manner that takes into account the value or volume of business generated between the parties, including Federal health care program business.

* * *

Percentage compensation arrangements are potentially abusive, however, because they provide financial incentives that may encourage overutilization of items and services and may increase program costs.⁶²

Although failure to meet a safe harbor does not necessarily mean an arrangement is unlawful under the AKS, in light of OIG’s consistent disapproval, molecular laboratories enrolled in federal health programs should consider alternatives to commission-based compensation if they choose to market their lab services through independent contractors. Start-up lab companies unable to bear the expense of an employee sales force may have great difficulty launching novel molecular testing without the option to contract and compensate an outside sales force on the basis of sales volume.

Note that certain states also expressly prohibit labs from contracting with independent contractors to sell lab testing.⁶³

Alternatives to percentage-based structures tied to volume or value of lab testing may include fair market value compensation that is set in advance and is based upon other production-related values not determined by volume or value of lab referrals that result from the contractor's marketing activities, such as (1) time spent, (2) numbers of attendees at marketing presentations, (3) number of sales presentations made, (4) overall financial performance of a region or division of the lab organization, or (5) achievement of pre-set financial performance targets not linked to specific customers or test volumes. Any such methodologies should be carefully spelled out in the written personal services agreement between the lab and the contractor.

3. Business Practices Involving the Ordering Provider.

As explained above, to build the case for carrier reimbursement of new molecular tests, a molecular lab must be able to demonstrate both clinical utility and clinical effectiveness of the new testing modalities, both of which depend in great measure on the success of the laboratory's marketing and educational activities with providers who will order the testing:

In simplest terms, it is typically pathologists and clinical laboratory professionals who educate doctors about the availability of new clinical lab tests and how to use them in their practice of medicine....the medical laboratory provides physicians with information on when to order these new assays, how to interpret the lab test results, and how to use those results to determine the most appropriate therapy.⁶⁴

Although federal and state laws governing labs impose limitations upon the laboratory's use of numerous conventional business development and customer relations practices used in other industries to promote new products and services (such as professional courtesy, free trials, and gifts and meals and

entertainment), in this article we have focused on three of the more challenging questions faced by new molecular labs: *Is it ok for a molecular lab to pay clients for specimen collection and processing? Is it ok to offer discounts on expensive molecular testing? Is it ok for an out-of-network molecular lab to cap or adjust patient co-payments and deductibles?*

a. Paying Clients for Specimen Collection and Processing.

New molecular tests can require specialized and labor-intensive patient specimen collection and processing methods. Unlike established laboratories, new molecular laboratories may encounter resistance by providers to adopting a new molecular test because of the added burden of collecting and submitting a patient's laboratory specimen. Established labs already may have collection stations in convenient proximity to their customers,⁶⁵ or they may place their own staff within a client's office,⁶⁶ these alternatives often are not feasible for a start-up laboratory due to logistical and cost constraints. As a result, the parties may propose instead to have the lab reimburse the provider for performing the specimen collection and processing. This arrangement gives rise to particular challenges under both the AKS and the Stark law, however.

Specifically, in its 2005 Advisory Opinion,⁶⁷ OIG concluded that a lab's payment to a physician customer of a fee of \$3 to \$6 per patient for collecting specimens from Medicare patients (using blood drawing supplies supplied at no charge by the lab), ran the risk of violating the AKS. "Particularly when viewed in the aggregate, this compensation provides an obvious financial benefit to the

referring physician, and it may be inferred that this benefit would be in exchange for referrals to the Lab.”⁶⁸

As further evidence of the federal government’s disapproval of the practice, the Department of Justice reported in November 2010 that Ameritox, a national toxicology laboratory, paid \$16.4 million to resolve a *qui tam* lawsuit, including claims, among others, that Ameritox had “paid cash kickbacks to its client physicians to induce them to refer Medicare reimbursable drug testing business to the lab.”⁶⁹ In a public statement, Ameritox said the money was for administrative work “related to specimen processing for Ameritox’s specialized testing.”⁷⁰

b. Pricing

The question of how to properly price molecular lab testing to the various purchasers of that testing, including clients and their patients, challenges even experienced lab industry participants. The existence of numerous different fee schedules adds complexity to price competition in the clinical laboratory marketplace.

Medicare Part B pays laboratories for a covered test at the lowest of: (1) the Medicare fee schedule, (2) the national payment limitation amount (fee cap), or (3) the lab’s actual charge. As a result, most labs set a standard fee schedule (above the Medicare fee schedule) for third-party and patient billing, and charge Medicare at that fee schedule, even though Medicare pays at the lower Medicare fee schedule.

Two different federal statutes are implicated when a lab determines to sell lab testing at a price that is below the Medicare clinical laboratory fee schedule--the Medicare “usual charge” rule and the federal AKS.

Under federal statute, a provider may be excluded if its charges to Medicare or Medicaid are “substantially in excess of its usual charges.”⁷¹ Historically, many labs have charged certain types of customers, such as hospitals, other laboratories and physicians, lower prices than they charge to Medicare. On several occasions, OIG has tried to define what level of pricing would violate the “usual charge” rule. OIG stated in a 2000 letter that “we do not believe that the [the rule] is implicated unless a provider’s charge to Medicare is substantially in excess of its median non-Medicare/Medicaid charge. In other words, a provider need not even worry about [the rule], unless it is discounting close to half of its non-Medicare/Medicaid business.”⁷² OIG also proposed a regulation in 2003 that was withdrawn in 2007,⁷³ leaving the application of the statute uncertain.

OIG has interpreted the AKS to prohibit discounts that are tied to referrals of federal program business or that are offered as a “swap” for more profitable federal program business. In a 1999 Advisory Opinion,⁷⁴ OIG concluded that a lab’s billing referring physicians directly at discounted (below cost) rates for pathology laboratory services might violate the AKS because OIG felt there was an improper nexus between the discount for private pay work and federal program referrals. OIG set forth a test for evaluating lab discounts:

[D]iscounts on [client] account billing business that are particularly suspect include, but are not limited to: discounted prices that are below the

laboratory's cost, and discounted prices that are lower than the prices that the laboratory offers to a buyer that (i) generates a volume of business for the supplier that is the same or greater than the volume of account billing business generated by the physician, but (ii) does not have any potentially available Federal health care program business.⁷⁵

Taken together, the federal guidance, although less than clear, indicates that molecular labs should (1) be judicious in offering discounts below the Medicare fee schedule, (2) make certain that any discounted prices exceed the lab's costs, and (3) avoid "swapping" discounted testing to get higher federal program rates.⁷⁶

Several states also have enacted laws that may restrict a laboratory's choice to bill lab testing at a reduced price, including state law limitations on billing identified above. For example, California's Attorney General and other enforcement agencies have interpreted California's Medicaid (Medi-Cal) law to prohibit labs from charging Medi-Cal more for services than any other purchaser. Seven California labs paid in excess of \$300,000, collectively, to settle a state law false claims action alleging violation of that Medi-Cal provision.⁷⁷

c. Patient Co-payment and Deductibles.

One additional challenge for molecular laboratories may arise when a lab performs and bills molecular testing performed on behalf of patients insured under private insurance plans with which the lab is a non-contracted provider. As an out-of-network lab, the lab may nonetheless receive payment from these insurance plans as an out-of-network provider, although often at a different amount than in-network laboratories. The lab must then respond to the insurers' unilateral condition that, as a non-contracted provider, the lab must assess and

collect from the patient a “co-payment” or “deductible,” that may assess the patient with an additional “premium” or “penalty” for obtaining lab services outside of the insurers’ network of preferred and contracted providers. The legal responsibility of a non-contracted lab to assess such a penalty against the patient has been the topic of recurrent and unresolved debate among private insurers, referring providers, patients and laboratories, contracted or non-contracted.

The election to waive or cap the patient assessment often poses a significant dilemma for molecular labs that have yet to establish provider agreements with many insurers, and therefore are left to bill for often costly molecular testing as an out-of-network provider. Compounding the question, as discussed above, is the resistance of many private (and government) insurers to granting coverage to new and highly specialized molecular tests, resulting in a greater likelihood of patients receiving bills for non-covered testing. Both the unpredictability of reimbursement and the relatively high cost of specialized molecular testing may result in even greater patient confusion and resistance to paying often unanticipated lab bills. Although insurers have challenged the decision by some labs to adjust or cap the patient charge in such circumstances,⁷⁸ laboratories may remain uncertain what their legal obligation is to pursue collection of these amounts, if any.

Federal guidance pertaining to waiver of Medicare co-pays is relatively straightforward, but it does not address the issue of private insurance out-of-network charges. As early as 1991, OIG cautioned that routine waiver of Medicare Part B deductibles and copayments by charge-based providers,

practitioners or suppliers is unlawful because it results in (1) false claims, (2) violations of the anti-kickback statute, and (3) excessive utilization of items and services paid for by Medicare,⁷⁹ However, neither the Medicare Part B nor Medicaid reimbursement for lab testing presently involves a patient co-payment.

Likewise, HIPAA authorizes the imposition of civil monetary penalties under the AKS for offering or providing to a federal program beneficiary any remuneration “that such person knows or should know is likely to influence [the beneficiary] to order or receive from a particular provider...any item or service” reimbursable by the federal programs.⁸⁰ Remuneration is defined to include “the waiver of coinsurance and deductibles,” but the definition specifically does not include waivers of co-payments and deductibles that are (1) neither offered as part of an advertisement or solicitation, (2) nor offered on a routine basis, but after a good faith determination of financial need, or after making reasonable collection efforts.⁸¹

Because the foregoing authority is limited on its face to federal program beneficiary co-payments and deductibles, its application, if at all, to obligations of a non-contracted laboratory to a private health insurer is unclear. More relevant may be the OIG’s discussion of “Waiver of Charges to Managed Care Patients,” in its 1994 *Special Fraud Alert: Special Arrangements for the Provision of Clinical Lab Services*.⁸² That advisory focused on a practice much like the waiver by a non-contracted lab of some or all of an insurance charge, discussed here; namely, the practice of non-contracted laboratories’ waiving lab charges in response to the practice of private managed care plans requiring that their

participating physicians and providers “use only the laboratory with which the plan has negotiated a fee schedule. In such situations, the plan usually will refuse to pay claims submitted by other laboratories. The provider, however, may use a different laboratory and may wish to continue to use that laboratory for non-managed care patients.”⁸³ OIG cautioned:

In cases where the provision of free services results in a benefit to the provider, the anti-kickback statute is implicated. If offered or accepted in return for the referral of Medicare or State health care plan business, both the laboratory and the physician may be violating the anti-kickback statute. There is no statutory exception or “safe harbor” to immunize any party to such a practice because the Federal programs do not realize the benefit of these “free” services.⁸⁴

OIG then explained that one primary issue in its anti-kickback analysis is whether the practice results in a benefit to the ordering provider, presumably beyond the benefit of choosing which laboratory to use: “The status of such agreements under the anti-kickback statute depends in part on the nature of the contractual relationship between the managed care plan and its providers.”⁸⁵ In the case of the managed care plans, OIG noted that under some managed care contracts the ordering provider would receive a bonus or incur a penalty based upon its compliance with the insurer’s utilization limits for lab testing.⁸⁶

The guidance, to the extent it can be applied to waiver by non-contracted lab of charges to private insurance patients generally, and not only managed care patients, suggests that OIG’s analysis would focus on whether the waiver results in a financial benefit to the ordering practitioner.

II. CONCLUSION

Although the growth and promised health benefits of personalized medicine likely will coax some great clarity and flexibility within the regulatory framework surrounding molecular laboratory testing, the influx of new and nontraditional participants, as well as heightened concerns about health care fraud and abuse, the regulatory climate will continue to be rigorous and complicated. Likewise, experience has shown that as the frequency of high priced testing increases, the standards for assessing medical necessity are likely to tighten. Legal counsel for the ever-expanding array of participants in the development and delivery of molecular laboratory testing will benefit from a deeper grasp of the specifics of the existing and evolving rules governing this rapidly evolving science of personal medicine and molecular laboratory testing.

¹ Stuart A. Scott, Ph.D., *Personalizing medicine with clinical pharmacogenetics*, *Genetics in Medicine*, Vol. 13, No. 12, Dec. 2011.

² Molecular tests are regulated pursuant to 21 U.S.C. § 321(h).

³ *Id.*

⁴ *See*, 21 U.S.C. 513.

⁵ *See, Draft Guidance for Industry, Clinical Laboratories, and FDA Staff In Vitro Diagnostic Multivariate Index Assays* (hereinafter the “Draft IVDMA Guidance”); 71 Fed. Reg. 52800, et seq., Sept. 7, 2006.

⁶ *Draft IVDMA Guidance*, at 4.

⁷ 21 C.F.R. 864.4020(a).

⁸ *See, Guidance for Industry and FDA Staff Commercially Distributed Analyte-Specific Reagents (“ASRs”): Frequently Asked Questions*. 71 Fed. Reg. 52799-52800, Sept. 7, 2006.

⁹ *Draft IVDMA Guidance*, citing to 62 Fed. Reg. 62243, Nov. 21, 1997.

¹⁰ We discuss IVDMIAs below.

¹¹ *See*, 21 C.F.R. 809.10(e)(1)(iv) and (vi).

¹² 21 C.F.R. 809.30(e).

¹³ *See*, 76 Fed. Reg. 31615, June 1, 2011.

¹⁴ *See, Draft Guidance for Industry and FDA Staff-Commercially Distributed In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only: Frequently Asked Questions* (June 1, 2011). On the web at

<http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253307.htm> Last visited May 10, 2012.

¹⁵ On the web at

[http://www.cap.org/apps/cap.portal?_nfpb=true&cntvwrPtl_t_actionOverride=%2Fportlets%2FcontentViewer%2Fshow&_windowLabel=cntvwrPtl&cntvwrPtl%7BactionForm.contentReference%](http://www.cap.org/apps/cap.portal?_nfpb=true&cntvwrPtl_t_actionOverride=%2Fportlets%2FcontentViewer%2Fshow&_windowLabel=cntvwrPtl&cntvwrPtl%7BactionForm.contentReference%2F)

[7D=statline%2Fstat051211.html&_state=maximized&_pageLabel=cntvwr](#) Last visited May 11, 2012.

¹⁶ See also, Comments of Alberto Gutierrez, Ph.D., Director of the Office of In Vitro Diagnostics (OVID), reported in STATLINE, May 12, 2011. On the web at

<http://www.fda.gov/MedicalDevices/NewsEvents/SorkshopsConferences/ucm212830.htm>. Last visited May 10, 2012.

¹⁷ 21 C.F.R. 809.3.

¹⁸ FDA provided the following examples of IVDMIAs in its *Draft IVDMIA Guidance*, p. 4:

- Gene expression profiling assay for breast cancer prognosis;
- A device that integrates quantitative results from multiple immunoassays to obtain a qualitative “score” that predicts a person’s risk of developing a disease or condition;
- A device that integrates a patient’s age, sex, and genotype of multiple genes to predict risk of or diagnose a disease or condition.

¹⁹ Draft IVDMIA Guidance, at 4.

²⁰ Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. § 263(a)

²¹ See, *Quality, Regulation and Clinical Utility of Laboratory-developed Molecular Tests*, Agency for Healthcare Research and Quality, Department of Health and Human Services (2010).

²² 42 C.F.R. Part 493, subparts H and I.

²³ 42 C.F.R. Part 493, subpart K.

²⁴ 42 C.F.R. Part 493, subpart M.

²⁵ 42 C.F.R. Part 493, subpart Q.

²⁶ 42 C.F.R. Part 493, subpart R

²⁷ 42 U.S.C. § 263a(a).

²⁸ *Quality, Regulation and Clinical Utility of Laboratory-developed Molecular Tests, Technology Assessment Report, Product ID: LABC 0707*, p. 34-35 (2010).

²⁹ See, 42 C.F.R. 493.17 to .19; and 42 U.S.C. § 263a(d)-2 to 4.

³⁰ See, 42 C.F.R. 493.1236(c). 42 C.F.R. 493.1236 provides as follows:

- (a) The laboratory must review and evaluate the results obtained on proficiency testing performed as specified in subpart H of this part.
- (b) The laboratory must verify the accuracy of the following:
 - (1) Any analyte or subspecialty without analytes listed in subpart I of this part that is not evaluated or scored by a CMS-approved proficiency testing program.
 - (2) Any analyte, specialty or subspecialty assigned a proficiency testing score that does not reflect laboratory test performance (that is, when the proficiency testing program does not obtain the agreement required for scoring as specified in subpart I of this part, or the laboratory receives a zero score for nonparticipation, or late return of results).
- (c) At least twice annually, the laboratory must verify the accuracy of the following:
 - (1) Any test or procedure it performs that is not included in subpart I of this part.
 - (2) Any test or procedure listed in subpart I of this part for which compatible proficiency testing samples are not offered by a CMS-approved proficiency testing program.
- (d) All proficiency testing evaluation and verification activities must be documented.

³¹ See, *Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions*. (July 9, 2009). On the web at

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5806a1.htm> Last visited May 5, 2012.

³² 10 N.Y. Comp Codes R. & Regs. 10 § 58-1.01 (2012)

³³ Available on the web at: <http://www.ama-assn.org/resources/doc/cpt/ivdmia-workgroup-oct2011.pdf>

³⁴ See, Social Security Act, § 1862(a)(1)(A); 42 U.S.C. § 1395y(a)(1)(A).

³⁵ *Quality Regulation and Clinical Utility of Lab-developed Molecular Tests*, Agency For Healthcare Research and Quality, p. 22 (Oct. 6, 2010).

³⁶ Id. at 23.

³⁷ Id. at 25.

³⁸ Id. at 25.

³⁹ See, 45 C.F.R. § 160.102.

⁴⁰ 65 Fed. Reg. 50311, 50312, Aug. 17, 2000.

⁴¹ See, e.g., AMA, Multianalyte Assays with Algorithmic Analyses (Oct. 13, 2011). On the web at <http://www.ama-assn.org/resources/doc/cpt/ivdmla-workgroup-oct2011.pdf>. Last visited May 10, 2012.

⁴² See, 45 C.F.R. § 160.102.

⁴³ MLN Matters No. MM7654, at 3 (Dec. 9, 2011).

⁴⁴ 42 U.S.C. § 1320a-7b(b). Among other things, the AKS prohibits anyone from paying or receiving remuneration "in return for...arranging for or recommending purchasing, leasing or ordering any good, facility, service, or item for which payment may be made by in whole or in part under a Federal health care program."

⁴⁵ 42 U.S.C. § 1395nn.

⁴⁶ "PricewaterhouseCoopers, The new science of personalized medicine: Translating the promise into practice." (Oct. 2009).

⁴⁷ 42 U.S.C. § 1320a-7b(b). A fully-integrated legal entity typically will satisfy the AKS investment safe harbor to the extent See, 42 C.F.R. § 1001.952(a)(2) (investors in a position to make or influence federal program referrals may own no more than 40% of the entity; no more than 40% of gross revenue of the entity can come from federal program referrals or other business that is generated or influenced by investors in the entity; terms offered to investors must have no relation to previous or expected volume of federal program referrals, items, or services furnished by the investor). See, 42 C.F.R. § 1001.952(a)(2).

⁴⁸ Although the Stark law in-office ancillary services exception would permit the development of a CLIA high-complexity molecular lab owned and operated solely by the physician, or a physician group practice meeting the Stark law definition, it would not permit investment in an outside molecular lab organization by a physician from whom the lab receives federal program lab referrals to be billed by the lab. See, 42 C.F.R. § 411.355(b) and 42 C.F.R. § 411.352.

⁴⁹ 1989 OIG *Special Fraud Alert on Joint Venture Arrangements*. Note that this arrangement also likely violates the direct billing rule, discussed below. 59 Fed. Reg. 65372, Dec. 19, 1994

⁵⁰ OIG not only reprinted the 1989 *Special Fraud Alert* in its 1994 *Special Fraud Alert* (59 Fed. Reg. 65372, Dec. 19, 1994), it also issued a 2003 *Special Advisory Bulletin on "Contractual Joint Ventures"*. 68 Fed. Reg. 23148, April 30, 2003. OIG also has published numerous Advisory Opinions disapproving health care joint ventures, including two pathology lab ventures in 2004, and 2011. See, OIG Advisory Opinion No. 04-17 (Dec. 17, 2004), and OIG Advisory Opinion No. 11-15 (Oct. 11, 2011).

⁵¹ See, 42 U.S.C. § 13951 (h)(5)(A); and 42 U.S.C. § 1396a(a)(32).

⁵² Both the 70 percent and the "under arrangement" exceptions to the Medicare direct billing rule may add flexibility in ventures between two labs or between a hospital and an outside lab: (1) an independent lab enrolled in Medicare may bill Medicare for testing sent to another enrolled lab, so long as the referring lab performs on site at least 70 percent of all testing it receives annually; and (2) a hospital may bill Medicare for testing performed by an enrolled lab and provided to the enrolled hospital "under arrangement." 42 U.S.C. § 13951 (h)(5)(A)(iii).

⁵³ *Hanlester Network, et al., Melvin L. Huntsinger, M.D., Ned Welsh*, DAB No. 1347 (July 24, 1992).

⁵⁴ 42 C.F.R. Sections 493.2 and 493.1241.

⁵⁵ Examples include New York and New Jersey.

⁵⁶ Examples include Alabama, California, Florida, Maine, Maryland, Oregon and Washington.

⁵⁷ Examples include Arizona, Connecticut, Florida, Louisiana, Maine, Maryland, Oregon, Pennsylvania and Texas.

⁵⁸ 54 Fed. Reg. 3088, 3093, Jan. 23, 1989. See also, 42 U.S.C. § 1320a-7b(b)(3)(B).

⁵⁹ The Stark exception for *bona fide* employees, applies to referring physicians and their immediate family, and requires the employment to be for identifiable services; compensated in a manner that is consistent with the fair market value of the services and not determined in a manner that takes into account (directly or indirectly) the volume or value of any referrals by employee; and commercially reasonable even if no referrals were made to the employer.

⁶⁰ To meet the AKS safe harbor for personal services and management contracts, the sales agreement must: (i) be in writing and signed by the parties; (ii) specify the services to be performed; (iii) specify the schedule for any part-time services; (iv) be for a term of at least one year; (v) fix in advance the aggregate compensation, consistent with fair market value, and not determined in a manner that takes into account the volume or value of any federal program referrals; (vi) not include services involving the promotion of business that violates any federal or state law; and (vii) not include services not reasonably necessary to accomplish the commercially reasonable business purpose of the services. *See*, 42 C.F.R. § 1001.952 (d).

⁶¹ 1991 OIG Commentary. 56 Fed. Reg. 35952, July 29, 1991.

⁶² OIG Advisory Opinion No. 98-1 (March 25, 1998).

⁶³ NY Public Health Act § 587 (5); *See also*, *People v. Duz-Mor Diagnostic Laboratory, Inc.* 68 Cal.App.4th 654, 671 (CA 1998).

⁶⁴ Dark Daily Laboratory and Pathology News, *Changing Role for Pathology and Clinical Laboratory Testing Discussed at Personalized Medicine World Conference in Silicon Valley* (January 26, 2012). On the web at <http://www.darkdaily.com/changing-role-for-pathology-and-clinical-laboratory-testing-discussed-at-personalized-medicine-world-conference-in-silicon-valley-12512#axzz1uQrA2bCb> Last visited May 10, 2012.

⁶⁵ To the extent the lab leases such locations from a referring provider the lease must meet the under the AKS space rental safe harbor (42 C.F.R. 10001.952(b)), as well as the Stark law space rental exception if a physician is a party to the rental. 42 U.S.C. § 1395nn(e)(1)(B); 42 CFR § 411.357(a).

⁶⁶ A lab's placement of personnel within a physician practice solely to collect and process lab specimens to be tested by the lab is not a "compensation arrangement," so long as lab personnel do not perform services ordinarily provided by the physician's staff. *See*, CMS Commentary to Final Stark II Regulations. 66 Fed. Reg. 856, 948, Jan. 4, 2001. OIG has given similar limited approval in its OIG *Special Fraud Alert: Special Arrangements for the Provision of Clinical Lab Services* (Issued October 1994), 59 Fed. Reg. 65372, Dec. 19, 1994. Note that the practice is prohibited by certain states, however.

⁶⁷ OIG Advisory Opinion No. 05-08 (June 6, 2005).

⁶⁸ *Id.*

⁶⁹ (Dec. 7, 2011 Press Release, Department of Justice, "Middle District Of Florida Ranks First Nationally In The Number Of Civil Cases Defended And Fifth In The Recovery Of Money Defrauded From Federal Programs." On the web at www.justice.gov/usao/flm/press/2011/dec/20111207_CivilDivision.html Last visited May 14, 2012.

⁷⁰ Tampa Bay Times, "Drug-testing company to pay \$16.3 million to settle kickback claims," Nov. 17, 2010. On the web at <http://www.tampabay.com/news/business/corporate/drug-testing-company-to-pay-163-million-to-settle-kickback-claims/1134676> Last visited May 15, 2012.

⁷¹ Section 1128(b)(6)(A) of the Social Security Act, codified at 42 U.S.C. §1320a-7.

⁷² Letter dated April 26, 2000, from Kevin G. McAnaney, Chief, Industry Guidance Branch, HHS Office of Inspector General. On the web at <http://oig.hhs.gov/fraud/docs/safeharborregulations/lab.htm> Last visited May 14, 2012.

⁷³ *See*, 72 Fed. Reg. 33430, June 18, 2007.

⁷⁴ OIG Advisory Opinion 99-13 (Dec. 7, 1999).

⁷⁵ *Id.*

⁷⁶ U.S. Senators Grassley (R-Iowa) and Baucus (D-Mont.) announced in November 2011, that they are investigating "a practice where insurers receive discounted pricing from labs in exchange for referrals, including testing for Medicare beneficiaries." *Grassley, Baucus Scrutinize Practice by Health Insurers and Testing Labs*, November 08, 2011 Press Release. On the web at <http://www.finance.senate.gov/newsroom/chairman/release/?id=8be10208-a6e8-474b-89c7-3025badaac49> Last visited May 14, 2012.

⁷⁷ *See*, Office of the Attorney General, Department of Justice. State of California, Press Release, May 19, 2011, *Attorney General Kamala D. Harris Announces \$241 Million Settlement with*

Quest Diagnostic. On the web at http://oag.ca.gov/news/press_release?id=2518 Last visited May 14, 2012.

⁷⁸ See, “NonPar Lab Practices: Waiving or Capping Member Cost Share Prohibited,” UnitedHealthcare Network Bulletin, May 2012 (Vol. 49). On the web at <https://www.unitedhealthcareonline.com/b2c/CmaAction.do?channelId=01af50581693b010VgnVCM100000c520720a> Last visited May 14, 2012. See, also, *Trustmark Life Ins. Co. v. Univ. of Chi. Hosps.*, 207 F.3d 876 (7th Cir. 2000); *Kennedy v. Conn. Gen. Life Ins. Co.*, 924 F.2d 698, 699 (7th Cir. 1991).

⁷⁹ *OIG Special Fraud Alert: Routine Waiver of Copayments or Deductibles Under Medicare Part B* (Issued May 1991; republished in 1994), 59 Fed. Reg. 65372, Dec. 19, 1994.

⁸⁰ 42 U.S.C. § 1320a-7a (a) (5).

⁸¹ 42 C.F.R. § 1001.952(k).

⁸² *OIG Special Fraud Alert: Special Arrangements for the Provision of Clinical Lab Services* (Issued October 1994), 59 Fed. Reg. 65372, Dec. 19, 1994.

⁸³ *Id.*

⁸⁴ *Id.* (Emphasis added).

⁸⁵ *Id.*

⁸⁶ *Id.*

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