DEVELOPING ANTI-KICKBACK COMPLIANCE GUIDANCE AT THE INTERSECTION OF "SPONSORED" AND "GENETIC TESTING" PROGRAMS

Yasameen Joulaee†

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† J.D. Candidate, University of California, Berkeley, School of Law, 2026. My utmost gratitude to Professor Allison Schmitt for her continued guidance through all stages of drafting and beyond. An additional thank you to Lauren Katzeff, Wayne Stacy, Maya Darrow, and the Fall 2024 Law and Technology Writing Workshop student cohort.

I. INTRODUCTION

A patient experiencing symptoms of an undiagnosed health condition naturally seeks a diagnosis, regardless of its potential severity. Imagine that the patient has an opportunity to take an entirely free genetic test—in exchange for a blood or saliva sample—and to receive a diagnosis for their symptoms. A sponsoring company covers the cost of the test and coordinates the logistics with the physician and a third-party testing laboratory. Here, the test diagnoses potential genetic disorders. The patient might learn that they have a hereditary genetic mutation with a 10 percent chance of developing a disease. Alternatively, the patient might learn that they have a genetic disease, but there is an available medication that could reduce some of their symptoms. The patient might be comforted by receiving a diagnosis, devastated by the implications for their health, or relieved to have a treatment option.

If the patient receives a treatable diagnosis, the Office of Inspector General (OIG) concerns itself with how the patient can be offered medication treatment and by whom. The offer becomes especially suspect when companies sponsor genetic tests identifying the same conditions that they manufacture medications to treat. If the patient is insured through a federal healthcare program like Medicare or Medicaid, the government could be billed for the medication and subsequent care costs.

Economic and financial incentives underlying healthcare programs create vulnerabilities to overutilization costs and disrupt free market competition.[1] Congress enacted the Anti-Kickback Statute (AKS) in 1972 as a response to increasing fraud claims and growing Medicare and Medicaid costs.[2] Here, the AKS may flag the payment sponsoring genetic tests of fraudulent claims or Medicare and Medicaid costs. Any gamesmanship to induce the patient or the ordering physician into purchasing the medication conveniently manufactured by the sponsor would violate the AKS. The OIG applies the AKS broadly to any form of remuneration, or "anything of value."[3] While remuneration can take many forms, including cash, free rent, hotel stays, or meals, federal healthcare programs are predominantly antagonistic toward payments for referrals.[4]

1. *See* Richard P. Kusserow, *The Medicare & Medicaid Anti-Kickback Statute and the Safe Harbor Regulations—What's Next?*, 2 HEALTH MATRIX: J.L. & MED. 49, 52 (1992) (evaluating the economic incentives of referrals in the 1987 Social Security Act anti-kickback provisions).

2. Chinelo Diké-Minor, *The Untold Story of the United States' Anti-Kickback Laws*, 20 RUTGERS J.L. & PUB. POL'Y 103, 109–10 (2023).

3. *Fraud & Abuse Laws*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., https://oig.hhs.gov/compliance/physician-education/fraud-abuse-laws/.

4. *Id.*

The AKS seeks to protect patients from prescriptions improperly induced by sponsors or medication manufacturers. Still, the AKS does not cover every potential concern in offering a sponsored genetic test. First, the AKS does not evaluate the actual test results and the substantive impact that those results could have on a patient's health. The patient is likely not concerned with the behind-the-scenes operation of the sponsored program. Instead, the patient is concerned with the validity of the test results and the availability of treatment options—regardless of who manufactures it. Second, the OIG lacks a mechanism for considering the positive impact that sponsored genetic testing programs offer the healthcare industry. The patient can confirm a hereditary condition or develop a heightened awareness of early-onset symptoms. The physician can diagnose the disorder or establish a monitoring plan for an at-risk patient.

The genetic test and subsequent sponsored program are regulated the entire time it is available on the market. The Food and Drug Administration (FDA) analyzes the safety and efficacy of products throughout their lifecycle, including genetic tests.[5] The FDA provides the initial approval that the test is permissible for patient use. The OIG then enforces the AKS after the provider bills treatment costs arising from the sponsored test results to a federal healthcare program. Thus, the FDA regulates the genetic test, while the OIG regulates the sponsored program. Federal regulatory agencies simultaneously oversee sponsored genetic testing programs through distinct practices. Pharmaceutical manufacturers establishing a program must aggregate each agency's guidance and piecemeal its policies with no guarantee of compliance. Thus, federal regulatory agencies must jointly devise a comprehensive guidance document for sponsored genetic testing programs to wholly evaluate both the financial and practical implications.

This Note takes a holistic view of the sponsored genetic testing landscape and bridges the isolated components of "sponsored" and "genetic testing" under one comprehensive compliance framework. This Note seeks to avoid employing the AKS as a fallback to impose sanctions on gamesmanship behavior. Rather, this Note identifies the FDA and the OIG as the appropriate regulatory conciliators and suggests evidentiary factors to strengthen regulatory compliance guidance. Part II describes the FDA and the OIG agencies and their existing mechanisms that guide industry compliance. Part III summarizes two relevant, contrasting outcomes—the OIG Advisory Opinions ("AO 22-06" and "AO 24-12") and the *Ultragenyx* Settlement

5. *Quality and Compliance (Medical Devices)*, FDA, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/quality-and-compliance-medical-devices (last updated Jan. 31, 2024).

Agreement—then discusses the regulatory rationale for reaching those outcomes. Part IV proposes a collaborative regulatory framework tailored to pharmaceutical manufacturers establishing sponsored genetic testing programs and explores the practical and policy implications of applying such a framework. Part V concludes.

II. SPONSORED GENETIC TESTING IN REGULATORY CONTEXTS

Sponsored genetic testing programs are subject to regulatory compliance. The United States Department of Health and Human Services (HHS) is the supervisory regulatory agency that oversees both the FDA and the OIG. The FDA and OIG each have distinct roles in regulating sponsored genetic testing programs, as evidenced by their objectives, enforcement initiatives, and guidance documents. Section II.A reviews the HHS's organizational structure. Section II.B summarizes the FDA's objectives and its regulation of medical devices, including genetic tests. Section II.C outlines the OIG's objectives, AKS enforcement, and compliance guidance for pharmaceutical manufacturers.

A. ORGANIZATIONAL STRUCTURE: THE HHS OVERSEES THE FDA AND THE OIG

The HHS is the overarching agency that supervises initiatives protecting the health and well-being of Americans.[6] The Secretary is the highest authority role within the HHS.[7] Under the Secretary, the organization bifurcates into two main groups: the Office of the Secretary and the Operating Divisions.[8]

The Office of the Secretary oversees HHS programs, including the OIG.[9] The thirteen Operating Divisions administer a variety of health and human services and research initiatives, including the FDA.[10]

B. FOOD AND DRUG ADMINISTRATION (FDA)

The FDA is the primary agency responsible for ensuring the safety and effectiveness of food and drugs, though genetic tests are included within the

6. *HHS Organizational Charts Office of Secretary and Divisions*, U.S. DEP'T OF HEALTH & HUM. SERVS., https://www.hhs.gov/about/agencies/orgchart/index.html (last reviewed Sep. 19, 2024).

7. *Id.*; *HHS Agencies & Offices*, U.S. DEP'T OF HEALTH & HUM. SERVS., https://www.hhs.gov/about/agencies/hhs-agencies-and-offices/index.html.

8. *HHS Organizational Charts Office of Secretary and Divisions*, U.S. DEP'T OF HEALTH & HUM. SERVS, *supra* note 6.

9. *HHS Agencies & Offices*, U.S. DEP'T OF HEALTH & HUM. SERVS., *supra* note 7.

10. *Id.*

FDA's oversight as medical devices.[11] This Section explores how the FDA regulates genetic tests through its premarket approval pathways and provides an overview of the agency's collaborative regulatory initiatives.

1. Agency Objectives

The FDA is the nation's oldest consumer protection agency.[12] In 1906, the Pure Food and Drugs Act established the FDA to oversee food and drugs.[13] In 1976, Congress established comprehensive medical device regulation through the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act.[14] The Act delineated a three-class risk-based classification system, safety and effectiveness performance standards, and regulatory pathways for new medical devices.[15] Through its regulatory oversight, the FDA seeks to promote the development and manufacture of high-quality medical devices.[16]

2. Medical Device Regulation

The FDA's classification system for medical devices clearly outlines the standards and pathways for premarket approval.[17] However, genetic tests do not neatly fit into any single class; instead, the FDA has variably regulated genetic tests as different classes, created special guidance for certain tests, and, in some cases, exempted genetic tests from pre-approval altogether.

a) A Three-Class, Risk-Based Classification System

The 1976 Medical Device Amendments comprise the same three-class classification system in effect today.[18] Classes I through III are ranked in order of increasing risk and regulatory oversight.[19]

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11. *Direct-to-Consumer Tests*, FDA, https://www.fda.gov/medical-devices/in-vitro-diagnostics/direct-consumer-tests (last updated Dec. 20, 2019).

12. *A History of Medical Device Regulation & Oversight in the United States*, FDA, https://www.fda.gov/medical-devices/overview-device-regulation/history-medical-device-regulation-oversight-united-states (last updated Aug. 21, 2023).

13. *Id.*

14. *Id.*

15. Medical Device Amendments of 1976, Pub. L. No. 94-295, § 513(a)(1)(A)–(C), 90 Stat. 539, 540–41.

16. *Quality and Compliance (Medical Devices)*, FDA, *supra* note 5.

17. *How to Study and Market Your Device*, FDA, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/how-study-and-market-your-device (last updated Oct. 12, 2023).

18. *A History of Medical Device Regulation & Oversight in the United States*, FDA, *supra* note 12.

19. AMANDA K. SARATA, CONG. RSCH. SERV., R47374, FDA REGULATION OF MEDICAL DEVICES 3 (2023); *Overview of Device Regulation*, FDA, https://www.fda.gov/medical-

Across all three classes, every medical device is subject to compliance with general controls to uphold a standard of safety and effectiveness.[20] Some Class I and most Class II devices require a 510(k) premarket notification.[21] A 510(k) is a premarket submission to the FDA that demonstrates a device is safe and effective by being "substantially equivalent," or having the same design and purpose as another already approved (predicate) device.[22] If the FDA determines that substantial equivalence is met, the device is cleared for marketing under the same class and regulatory controls as the predicate device.[23]

The De Novo classification request is an alternate pathway to seek regulatory approval for medical devices when there are no legally marketed predicate devices.[24] The FDA determines De Novo eligibility by first verifying that there are no predicates, comparing the device to legally marketed devices.[25] Next, the FDA performs a substantive review.[26] If the FDA grants a De Novo request, the device will be assigned a new classification regulation for the new device type.[27] The De Novo pathway allows devices without predicates to enter the market as Class I or Class II devices, which are subject to fewer requirements than presumptively assigned, strictly regulated Class III devices.[28] Additionally, devices awarded De Novo classifications can serve as predicates for new devices of the same type in future premarket notifications.[29]

b) Genetic Tests as Medical Devices

Genetic tests pose a unique challenge to FDA regulation based on their intermediate status as products that can be simultaneously offered as services. For example, genetic tests can be regulated as "in vitro diagnostic" (IVD)

devices/device-advice-comprehensive-regulatory-assistance/overview-device-regulation#:~:text=Quality%20System%20Regulation%20(QS%20regulation,compliance%20with%20the%20QS%20requirements; *see also* 21 U.S.C. § 360(c)(a)(1)(A)–(C).

20. SARATA, *supra* note 19, at 6.

21. *How to Study and Market Your Device*, FDA, *supra* note 17.

22. *Premarket Notification 510(k)*, FDA, https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/premarket-notification-510k (last updated Aug. 22, 2024); Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 513(a)(4).

23. SARATA, *supra* note 19, at 9.

24. *De Novo Classification Request*, FDA, https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/de-novo-classification-request (last updated Oct. 4, 2022).

25. *Id.*

26. *Id.*

27. *Id.*

28. SARATA, *supra* note 19, at 4–5.

29. *Id.* at 5.

products by individually considering the reagents used to make diagnoses.[30] Reagents (and their risks) vary from Class I to Class III devices, and the FDA may regulate reagents as "restricted devices," placing specific restrictions on their sale, distribution, and use.[31] Reagents are necessary to perform a genetic test, subsequently impacting genetic test regulation and marketing.

The FDA has also issued multiple orders and industry guidance documents advising on medical device classifications for specific genetic test systems. However, the variable guidance, compounded with the 510(k) and De Novo pathways, makes anticipating the appropriate submission pathway a challenging and unpredictable feat for manufacturers. For example, in November 2017, the FDA issued an order exempting autosomal recessive carrier screening gene mutation detection systems from the 510(k) requirement if a misdiagnosis would not be associated with high morbidity or mortality.[32] Conversely, the FDA issued separate Class II Special Controls Guidance for breast cancer prognosis test systems and cardiac allograft gene expression profiling test systems.[33] Special controls guidance documents are developed to address the specific health risks associated with a test system.[34] Both guidance documents channel the genetic test systems through the 510(k) submission process, contradicting the 510(k) exemption ordered for the autosomal recessive carrier screening system.[35] Lastly, in September 2023, the FDA granted De Novo authorization for an IVD test that detects genetic variants associated with an elevated risk of developing certain cancers.[36] These examples illustrate how the premarket submission pathway is highly particular

30. Gail H. Javitt, *In Search of a Coherent Framework: Options for FDA Oversight of Genetic Tests*, 62 FOOD & DRUG L.J. 617, 619–20 (2007).

31. *Id.* at 620–21.

32. FDA Medical Devices, 82 Fed. Reg. 51567, 51569 (Nov. 7, 2017) (to be codified 21 C.F.R. pt. 866); *see also Class I and Class II Device Exemptions*, FDA, https://www.fda.gov/medical-devices/classify-your-medical-device/class-i-and-class-ii-device-exemptions (last updated Feb. 23, 2022) (on file with author).

33. FDA, CTR. FOR DEVICES & RADIOLOGICAL HEALTH (CDRH), GENE EXPRESSION PROFILING TEST SYSTEM FOR BREAST CANCER PROGNOSIS-CLASS II SPECIAL CONTROLS GUIDANCE FOR INDUSTRY AND FDA STAFF (2007); FDA, CDRH, CARDIAC ALLOGRAFT GENE EXPRESSION PROFILING TEST SYSTEMS-CLASS II SPECIAL CONTROLS GUIDANCE FOR INDUSTRY AND FDA STAFF (2009).

34. FDA, CDRH, CARDIAC ALLOGRAFT GENE EXPRESSION, *supra* note 33.

35. *Id.*; FDA, CDRH, GENE EXPRESSION PROFILING TEST SYSTEM FOR BREAST CANCER PROGNOSIS, *supra* note 33.

36. Press Release, FDA, FDA Grants First Marketing Authorization for a DNA Test to Assess Predisposition for Dozens of Cancer Types (Sep. 29, 2023), https://www.fda.gov/news-events/press-announcements/fda-grants-first-marketing-authorization-dna-test-assess-predisposition-dozens-cancer-types.

to the type of genetic test, arriving at different classification levels subject to different regulatory requirements.

In May 2024, the FDA issued a final rule amending the Federal Food, Drug, and Cosmetic Act to recognize IVDs as devices explicitly.[37] The rule focuses on the safety and effectiveness of laboratory developed tests (LDTs), a type of IVD designed, manufactured, and produced within a single laboratory for clinical use.[38] Large laboratories widely use LDTs in high volumes and frequently rely on them for critical healthcare decisions.[39] Before the rule, companies could market genetic tests as LDTs without FDA review.[40] Now, the FDA estimates that approximately 95 percent of IVDs will be Class I and II devices under the final rule.[41] This shift reflects the FDA's recognition that genetic test regulations require closer regulatory attention and statutory reform. Nonetheless, the FDA continues to regulate genetic tests diversely, where even classification as an LDT can profoundly impact the premarket requirements.

3. Specialized Task Force Programs

The FDA has several initiatives that should be leveraged to reform its varied approach to genetic test regulation. The FDA should use collaborative communities to stay informed about industry-wide sponsored genetic testing concerns and advance its robust fraud program to detect suspect sponsored programs.

a) Collaborative Community Initiative

The FDA's Center for Devices and Radiological Health (CDRH) established the "Collaborative Community" as a forum for public and private sector members to solve medical device challenges and achieve shared goals.[42]

37. FDA In Vitro Diagnostic Medical Devices, 89 Fed. Reg. 37286 (May 6, 2024) (to be codified at 21 C.F.R. pt. 809).

38. *Laboratory Developed Tests*, FDA, https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests (last updated Oct. 30, 2024).

39. *Id.*

40. *Genetic Non-Invasive Prenatal Screening Tests May Have False Results: FDA Safety Communication*, FDA, https://www.fda.gov/medical-devices/safety-communications/genetic-non-invasive-prenatal-screening-tests-may-have-false-results-fda-safety-communication (last updated Apr. 19, 2022) (on file with the Berkeley Tech. L.J.); *see also FDA Issues Warning About Risks of Noninvasive Prenatal Screening*, HEALIO (Apr. 20, 2022), https://www.healio.com/news/primary-care/20220420/fda-issues-warning-about-risks-of-noninvasive-prenatal-screening.

41. Brittany Schuck, Deputy Off. Dir., *FDA's Total Product Lifecycle Approach to IVDs Webinar*, FDA (Oct. 24, 2024), https://www.fda.gov/media/183011/download?attachment.

42. *Collaborative Communities: Addressing Health Care Challenges Together*, FDA, https://www.fda.gov/about-fda/cdrh-strategic-priorities-and-updates/collaborative-communities-addressing-health-care-challenges-together (last updated Sep. 20, 2024).

Each collaborative community concentrates on a specific topic, such as standardizing laboratory practices in pharmacogenomics.[43] The CDRH is not the manager or controller of collaborative communities; rather, the CDRH can be a participating member that fosters community and encourages broad and fair representation.[44] Other members may include patients, academics, healthcare professionals, federal and state agencies, international regulatory bodies, and industry.[45] Members have a collective interest in working together when "challenges are ill-defined or there is no consensus on the definition of the challenges."[46] Complex or prior failed efforts to address challenges, interrelated partners, and optimization interests are all driving factors that benefit from a collaborative community.[47]

The Collaborative Community initiative has several successful programs where an external stakeholder manages the community, and the FDA participates as a member. The National Evaluation System for health Technology (NEST) leverages real-world experience and advanced analytics data to map medical device total product life cycles, informing both pre- and post-market regulatory decisions.[48] NEST aims to improve the quality of evidence that healthcare providers and patients use to make treatment decisions and foster medical device innovation while assuring safety.[49] The NEST Coordinating Center (NESTcc) collaborative community was created to reduce the time and cost of data collection while increasing the value and reach of evidentiary findings.[50] Members promote standards, monitor progress, and govern the NEST ecosystem.[51] The NESTcc collaborative community is a textbook example that invites stakeholders to optimize how medical devices are employed across healthcare.

43. *Id.*

44. *Id.*; FDA, CDRH, 2018-2020 STRATEGIC PRIORITIES at 17 (Jan. 2018), https://www.fda.gov/media/110478/download?attachment.

45. *Collaborative Communities: Addressing Health Care Challenges Together*, FDA, *supra* note 42.

46. *Id.*

47. *Id.*

48. *National Evaluation System for Health Technology (NEST)*, FDA, CDRH, https://www.fda.gov/about-fda/cdrh-reports/national-evaluation-system-health-technology-nest (last updated Oct. 29, 2019).

49. *Id.*

50. *FDA in Brief: FDA Announces Participation in First Two 'Collaborative Communities' Working to Develop Solutions to Medical Device Innovation Challenges*, FDA, https://www.fda.gov/news-events/fda-brief/fda-brief-fda-announces-participation-first-two-collaborative-communities-working-develop-solutions (last updated Mar. 3, 2021).

51. *Id.*

Similarly, the "Case for Quality" collaborative community seeks to promote a competitive marketplace that values high-quality medical devices.[52] The initiative was formed after the FDA identified common manufacturing risks that impacted product quality but vastly improved compliance and reduced complaints and corrective actions once managed.[53] The Case for Quality objectives include identifying manufacturers that consistently produce high-quality medical devices in compliance with FDA regulations.[54] Successful manufacturing practices are identified and shared to support other manufacturers in improving their product quality.[55] Thus, manufacturers identified by the Case for Quality initiative serve as benchmarks for compliance, quality, and innovation in medical devices, streamlining FDA premarket submissions and marketization.

b) Pharmaceutical Fraud Program (PFP)

The FDA established the Pharmaceutical Fraud Program (PFP) in 2010 to detect, prosecute, and prevent pharmaceutical, biologic, and medical device fraud.[56] As part of the FDA, the PFP supports the Office of Criminal Investigations (OCI) and the Office of General Counsel Food and Drug Division (OGC-FDD) in investigating criminal violations of federal healthcare and anti-fraud statutes.[57] The PFP gathers information from both FDA and non-FDA resources concerning fraudulent marketing schemes, application and clinical trial fraud, and blatant manufacturing violations.[58] The program's primary goal is to detect and prosecute fraudulent conduct early, enabling the FDA to impede potential public harm from medical products that reach the market without following the appropriate FDA approval processes.[59] By restricting noncompliant medical products from reaching the market and consumers, the PFP saves healthcare programs from unnecessary

52. *Case for Quality*, FDA, https://www.fda.gov/medical-devices/quality-and-compliance-medical-devices/case-quality (last updated July 29, 2020); FDA CTR. DEVICES & RADIOLOGICAL HEALTH, 2018-2020 STRATEGIC PRIORITIES, *supra* note 44, at 18.

53. *Case for Quality*, FDA, *supra* note 52.

54. *Id.*

55. *Id.*

56. KATHLEEN M. BOOZANG, CHARLES A. SULLIVAN & KATE GREENWOOD, THE FALSE CLAIMS ACT AND THE POLICING OF PROMOTIONAL CLAIMS ABOUT DRUGS: A CALL FOR INCREASED TRANSPARENCY 25 (2015); U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., ANNUAL REPORT OF THE DEPARTMENTS OF HEALTH AND HUMAN SERVICES AND JUSTICE: HEALTH CARE FRAUD AND ABUSE CONTROL PROGRAM FY 2022, at 101 [hereinafter HHS OIG 2022 ANNUAL REPORT].

57. HHS OIG 2022 ANNUAL REPORT, *supra* note 56.

58. *Id.*

59. *Id.*

expenditures.[60] The PFP seamlessly aligns with AKS motivations but takes a preemptive, regulatory approach.

In 2023, the PFP opened eleven criminal investigations, with three targeting fraudulent marketing practices.[61] The investigations concerned violations with severe public health consequences, including potential kickbacks by pharmaceutical sales representatives on the intended use of a drug.[62] However, complex fraud investigations require extensive document review and can span five years or more from initiation to conclusion.[63] Despite this, PFP investigations have nonetheless resulted in several successful prosecutions.[64]

C. OFFICE OF INSPECTOR GENERAL (OIG)

The OIG operates to detect and halt fraud and abuse in federal healthcare programs, as demonstrated by a lengthy history of congressional legislation. This Section will review the OIG's mechanisms to regulate sponsored genetic testing programs, focusing on the AKS and the 2003 Compliance Program Guidance for Pharmaceutical Manufacturers as its chief regulatory documents.

1. Agency Objectives

The OIG was established in 1976 and has long served as the nation's principal agent in combating waste, fraud, and abuse while improving the efficiency of Medicare, Medicaid, and other HHS programs.[65] However, the OIG's work also spans from advanced data analytics to cybersecurity matters.[66] In fiscal year 2023, the OIG allocated 23 percent of its efforts to Public Health, Science, and Regulatory Agency oversight, including the FDA.[67] The OIG focused the remaining 77 percent on Medicare and Medicaid oversight, which

60. *Id.*

61. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., ANNUAL REPORT OF THE DEPARTMENTS OF HEALTH AND HUMAN SERVICES AND JUSTICE, HEALTH CARE FRAUD AND ABUSE CONTROL PROGRAM FY 2023, at 94–95 [hereinafter HHS OIG 2023 ANNUAL REPORT].

62. *Id.* at 95.

63. *Id.*

64. *Id.*

65. *About OIG*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., https://oig.hhs.gov/about-oig/#:~:text=Who%20We%20Are,Human%20Services%20(HHS)%20programs. (The OIG performs "independent criminal and civil investigations, audits, evaluations, administrative enforcement actions, data analytics, and other activities to fulfill its mission.").

66. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., FACT SHEET, https://oig.hhs.gov/documents/root/1140/About-OIG-Fact-Sheet.pdf.

67. *Id.*

includes kickback enforcement in federal healthcare programs.[68] This imbalance demonstrates the OIG's focus on enforcement actions and recovery of misspent funds, which squarely aligns with the AKS objectives.

The OIG and the Department of Justice (DOJ) are primarily responsible for enforcing the AKS.[69] Kickbacks include any remuneration to induce or reward referrals of items or services payable by a federal healthcare program.[70] Under the AKS, individuals who offer or pay prohibited remuneration, and, on the other end, individuals who solicit or receive the prohibited remuneration are liable for kickbacks.[71]

The OIG aims to resolve uncertainties and interpret AKS requirements by issuing publicly accessible Advisory Opinions.[72] Advisory Opinions explore what constitutes remuneration under the AKS, determine whether an arrangement satisfies the AKS criteria for activities that do not result in prohibited remuneration, and assess whether an activity poses grounds for AKS sanctions.[73] Any requesting party can submit an advisory opinion request to the OIG via email and expect a response within ten business days.[74] While Advisory Opinions are only binding between the OIG and the requesting party for that particular agreement, they are indisputably a vital resource consistently consulted by health law practitioners.[75] Notice and Comment Rulemaking and Special Advisory Bulletins are other OIG-authored forms of interpretive guidance.[76] Case law provides a judicial review of the AKS; however, whistleblowers commonly file qui tam suits under the False Claims Act, where courts have been hesitant to find kickbacks from Medicare and Medicaid claims alone.[77]

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68. *Id.*

69. ADA JANOCINSKA & GEOFFREY KAISER, THE FEDERAL ANTI-KICKBACK STATUTE AND SAFE HARBORS 2 (2d ed. 2024).

70. *Drug Spending*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., https://oig.hhs.gov/reports-and-publications/featured-topics/drug-spending/guidance.asp (last updated Aug. 9, 2024).

71. HHS OIG Special Fraud Alert: Speaker Programs, 87 Fed. Reg. 51683 (Nov. 16, 2020).

72. JANOCINSKA & KAISER, *supra* note 69, at 4.

73. *Id.*

74. *Advisory Opinion Process*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., https://oig.hhs.gov/compliance/advisory-opinions/process/.

75. JANOCINSKA & KAISER, *supra* note 69, at 5.

76. *Id.*

77. *Id.*; Adam W. Overstreet & Matthew J. Kroplin, *The Causation Trend in Anti-Kickback False Claim Cases: Courts' Rejection of Relators' Taint Theory Should Cause Them Concern at the Summary Judgement Stage of Qui Tam Litigation*, 31 HEALTH L. 1, 1–5 (Oct. 2018).

2. Anti-Kickback Statute (AKS): 42 U.S.C. § 1320a-7b(b)

Congress established the Anti-Kickback Statute (AKS) in 1972 to combat fraud and abuse in healthcare costs.[78] Congress recognized that violations "adversely impact[ed] all Americans" by "cheat[ing] taxpayers," "divert[ing] from those most in need, the nation's elderly and poor," and "erod[ing] the financial stability" of state and local governments.[79] Nonetheless, by 1977, Congress discovered tremendous evidence of Medicare and Medicaid provider fraud and abuse, estimating over $1 billion in violations annually.[80] Thus, the Anti-Fraud and Abuse Amendments heightened AKS violations to a felony punishable by up to five years imprisonment and a maximum fine of $25,000.[81] Additionally, the AKS expanded to prohibit "*any* remuneration (including any kickback, bribe, or rebate) directly or indirectly, overtly or covertly, in cash or in kind."[82] In 1980, Congress narrowed the AKS to apply solely when the violation was done "knowingly and willfully."[83]

In *United States v. Greber*, the Third Circuit unpacked the term "remuneration," ruling that payment for services that were actually performed still counts as an AKS violation if it was in furtherance of business.[84] The *Greber* holding is discrete in its language, yet paramount in consequences: inducement of future referrals does not have to be the basis for payment—as long as it is *one* purpose of the arrangement, it is a violation.[85]

The OIG enacted AKS safe harbors in 1991, carving out ten "innocuous arrangements" that should not be prosecuted.[86] Additional safe harbors have been created and revised over the last thirty-three years to date.[87] Still, the true "safety" of these safe harbors is unclear, such as whether meeting all of the conditions of a safe harbor provision guarantees absolute protection from prosecution.[88] For example, the OIG stated in the preamble to the 1991 enactment that if a person fully complies with a safe harbor provision, they

78. Diké-Minor, *supra* note 2.

79. H.R. REP. NO. 95-393, at 44 (1977); 1977 U.S.C.C.A.N. 3039, 3047.

80. 123 CONG. REC. S16011 (1977).

81. Medicare-Medicaid Anti-Fraud and Abuse Amendments, Pub. L. No. 95-142, § 4, 91 Stat. 1175, 1179–83 (1977).

82. *Id.* (emphasis added).

83. Omnibus Reconciliation Act of 1980, Pub. L. No. 96-499, 94 Stat. 2599 (1980).

84. 760 F.2d 68, 69 (3d Cir. 1985).

85. Diké-Minor, *supra* note 2, at 113.

86. Final Rule: OIG Anti-Kickback Provisions, 56 Fed. Reg. 35952, 35957 (July 29, 1991).

87. *Safe Harbor Regulations*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., https://oig.hhs.gov/compliance/safe-harbor-regulations/.

88. Donald H. Romano, *How Safe Are the Safe Harbors: An In-Depth Look at Statutory and Regulatory Exceptions to the Anti-Kickback Statute*, 30 HEALTH L. 1 (Dec. 2017).

will not be prosecuted for the arrangement.[89] Likewise, each safe harbor provision states that "'remuneration' does not include" a certain arrangement, meaning if the safe harbor is met, there is no remuneration and therefore no AKS violation.[90] The "discounts" safe harbor excludes items or services paid for wholly or partially under federal healthcare programs from qualifying as remuneration.[91] Two courts have nonetheless said in dicta that a lack of intent is required to satisfy safe harbor provisions—meeting the provisions alone is not enough.[92] These decisions have blurred the objective criteria of safe harbor provisions by incorporating subjective intent considerations.[93] Safe harbors present challenges for program sponsors, who not only have to strictly adhere to the contours of a safe harbor provision but also anticipate variable judicial interpretation.

3. Compliance Program Guidance for Pharmaceutical Manufacturers

In 2003, the OIG issued compliance guidance for pharmaceutical manufacturers, outlining the fundamental elements to achieve an effective compliance program.[94] The guidance identifies "kickbacks and other illegal remuneration" as a specific risk area for pharmaceutical manufacturers to address during legal review and in the development of policies and procedures.[95]

The guidance instructs pharmaceutical manufacturers to identify liability risks under the AKS by framing a two-part test to identify arrangements with a significant potential for abuse: (1) identify any remunerative relationship between the manufacturer and those individuals or entities in a position to directly or indirectly generate federal healthcare business for the manufacturer, then (2) determine whether any one purpose of remuneration would induce a referral or recommendation for services at least partially payable by a federal healthcare program.[96] Even if a manufacturer satisfies this test, the guidance encourages further consideration of practices that courts have recognized as high-risk for prosecution.[97] Problematic practices include interfering with

89. *Id.* at 3; *see also* 56 Fed. Reg. at 35954.

90. 42 C.F.R. § 1001.952(a)–(jj).

91. 42 C.F.R. § 1001.952(h)(5)(ii).

92. *See* United States v. Shaw, 106 F. Supp. 2d 103 (D. Mass. 2000); United States *ex rel.* Westmoreland v. Amgen, Inc., 812 F. Supp. 2d 39 (D. Mass. 2011); *see also* Romano, *supra* note 88, at 3–4.

93. *See* Romano, *supra* note 88, at 3–4.

94. OIG Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23731 (May 5, 2003).

95. *Id.* at 23733.

96. *Id.* at 23734.

97. *Id.*

clinical decision-making, increasing costs to federal healthcare programs, increasing inappropriate or overutilization risks, and raising patient safety or quality of care concerns.[98]

The guidance advises manufacturers to review their arrangements in the totality of all facts and circumstances, even if they do not fit squarely within an AKS safe harbor.[99] Key considerations include the nature of the relationship between the parties (e.g., the manufacturer and the physician), how the remuneration is determined, the value of the remuneration and its potential impact on federal healthcare programs, and potential conflicts of interest.[100] While these considerations are adopted from the PhRMA Code on Interactions with Healthcare Professionals, compliance does not guarantee protection from AKS liability.[101] Nonetheless, the guidance still recognizes methods to substantially reduce fraud and abuse risks and demonstrate a good-faith effort to comply with federal healthcare laws.[102]

In April 2023, the OIG announced plans to publish updated industry segment-specific compliance program guidance documents.[103] In September 2024, the OIG that specified it anticipates publishing a pharmaceutical manufacturer-specific document with the release date to be determined, though guidance documents for other industries are planned through 2025.[104] In the interim, the compliance guidance from 2003 and recent cases are the best indicators of where the OIG stands on sponsored genetic testing programs.

III. OPPOSITE OUTCOMES IN SPONSORED GENETIC TESTING PROGRAMS

Two principal cases illustrate contrasting regulatory compliance holdings for sponsored genetic testing programs, where agencies determined if the disputed programs violated the AKS. Section III.A summarizes two OIG Advisory Opinions (AO 22-06 and AO 24-12). Section III.B outlines the *United States v. Ultragenyx* Settlement Agreement. Lastly, Section III.C reviews an outstanding DOJ investigation against BioMarin Pharmaceuticals, assesses

98. *Id.*
99. *Id.* at 23737.
100. *Id.*
101. *Id.*
102. *Id.*
103. *Compliance Guide*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., https://oig.hhs.gov/compliance/compliance-guidance/ (last updated Sep. 18, 2024).
104. *Id.*

regulatory implications following *Loper Bright*, and reflects on current industry concerns regarding sponsored genetic testing program regulations.

A. FAVORABLE OUTCOMES: OIG ADVISORY OPINIONS

The OIG has issued three Advisory Opinions addressing sponsored genetic testing programs.[105] Each Opinion illustrates a Requestor's program that was not sanctioned under the AKS. While the Requestors adequately mitigated fraud and abuse risks to avoid sanctions, the Opinions reflect how advisory opinions can be narrow in scope and lack reliability to draw broader compliance principles.

1. OIG Advisory Opinion 22-06 (AO 22-06)

The OIG wrote its first advisory opinion on sponsored genetic testing programs in AO 22-06. The OIG distinguished the program based on the genetic test's limited results and the Requestor's shielded marketing practices, finding that these safeguards were sufficient to avoid sanctions under the AKS.

a) Factual Background

The Requestor, a biopharmaceutical company, manufactures two FDA-approved medications that treat a disease deriving from a genetic disorder.[106] The disorder can present in different forms that are distinguishable by the bodily systems affected and the symptoms presented.[107] Here, the form of the disorder (the "disease") primarily impacts the heart and can lead to heart failure and death.[108] The disease can be inherited ("hereditary" form) or occur spontaneously ("spontaneous" form).[109] The Requestor manufactures two FDA-approved medications that each treat both forms of the disease by reducing cardiovascular-related hospitalizations and mortalities.[110] The Requestor's sole interest in manufacturing, marketing, or financing items or services that treat the disease centers on the medications.[111]

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105. The OIG continues to publish Advisory Opinions that align with the same analyses and outcomes discussed *infra* Section III.A. *See* U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., OIG ADVISORY OPINION NO. 25-07 (2025), https://oig.hhs.gov/documents/advisory-opinions/10472/AO-25-07.pdf. For the scope of this Note, only Advisory Opinions 22-06 and 24-12 are discussed.

106. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., OIG ADVISORY OPINION NO. 22-06, at 2 (2022) [hereinafter AO 22-06], https://oig.hhs.gov/documents/advisory-opinions/1028/AO-22-06.pdf.

107. *Id.*

108. *Id.*

109. *Id.* Note that the spontaneously developed form name is redacted in the AO, hence "spontaneous" is proposed as an abbreviated name.

110. *Id.*

111. *Id.*

i) The Genetic Test

The genetic test offered through the Requestor's sponsored program is insufficient on its own to diagnose the disease.[112] The genetic test must be ordered in parallel with other diagnostic tests to determine if the disease is present and to rule out other possible conditions.[113] Only after conducting these parallel tests can the genetic test results be used to identify the form of the disease present.[114]

The genetic test provides valuable results for three types of patients. First, previously diagnosed patients can learn if they have the hereditary or spontaneous form of the disorder, where the hereditary form may have a quicker expected disease progression.[115] Second, undiagnosed symptomatic patients can learn which form they have if the parallel test confirms a diagnosis.[116] Third, patients related to someone with the hereditary form can be made aware of whether they carry a gene mutation associated with the disease and seek monitoring by a cardiologist, potentially shortening the time from symptom onset to diagnosis.[117]

Healthcare providers thus employ the genetic testing program to supplement their evaluation, but the genetic test results alone are not a conclusive basis for prescribing the Requestor's medications.[118] The Requestor's medications are solely for patients with a confirmed diagnosis; the medications have not been approved for the prevention of the disease or treatment of undiagnosed patients.[119] To put this limitation in context, for a specific mutation that causes a majority of the hereditary form cases, only 10 to 20 percent of patients with that mutation will develop the disease.[120] Thus, many patients who test positive for a gene mutation may never develop the disease.[121] Even if a medication is ultimately required, the physician's prescription is not influenced by the genetic test results since both medications treat both forms of the disease.[122]

112. *Id.*
113. *Id.*
114. *Id.* at 2–3.
115. *Id.*
116. *Id.* at 3.
117. *Id.*
118. *Id.*
119. *Id.*
120. *Id.*
121. *Id.*
122. *Id.*

ii) The Sponsored Program

The Requestor's genetic testing program operates through an arrangement with a contracted third-party laboratory and a contracted third-party genetic counseling service.[123] The laboratory is responsible for developing and producing a customized specimen collection kit and conducting genetic tests for the program.[124] If a physician refers the patient to the optional counseling service, the laboratory provides patient information to the counseling vendor.[125] The Requestor never receives any individually identifiable patient health information.[126] Instead, the Requestor only receives aggregate monthly reports from the laboratory to track participation, again with de-identified information that complies with 42 C.F.R. § 164.514(b)(2) privacy standards.[127] The Requestor does not receive sufficient information to identify physicians who order tests through the program unless the physicians voluntarily disclose this information.[128]

iii) Requestor's Marketing

The Requestor restricts its sales force from accessing any data received from the laboratory or counseling vendors and does not use this data in its sales or marketing activities.[129] Instead, the Requestor identifies cardiologists who are likely to diagnose and treat patients with the disease.[130] The Requestor's sales representatives do not consider a physician's use of the program or their history of prescribing the Requestor's medication when distributing specimen collection kits.[131] Likewise, sales representatives have a limited number of specimen collection kits that can be distributed to any individual physician.[132]

Patients may learn about the sponsored genetic testing program through the Requestor's patient support program, which provides information after a patient has been prescribed one of the Requestor's medications.[133] Patients may also learn about the program through patient advocacy groups.[134] The

123. *Id.* at 4–5.
124. *Id.* at 4.
125. *Id.* at 5.
126. *Id.*
127. *Id.*
128. *Id.*
129. *Id.*
130. *Id.* at 6.
131. *Id.*
132. *Id.*
133. *Id.*
134. *Id.*

laboratory and counseling vendors are prohibited from promoting the Requestor's program or medications to patients and providers.[135]

b) OIG Opinion and Holding

In April 2022, the OIG issued AO 22-06, finding that the Requestor's sponsored genetic testing program implicated the AKS because it provided remuneration to both patients and their physicians, who may prescribe or induce patients to purchase the Requestor's medications.[136] However, for patients, the program provides free genetic testing and counseling services that are "inherently valuable."[137] For physicians, the program enables offering a service at no cost to them or their patients, albeit creating an opportunity to bill for additional services or expand their care in unrelated capacities.[138] Despite these concerns, the OIG held that the program posed a "sufficiently low risk of fraud and abuse" under the AKS for three primary reasons:

1. The program is unlikely to lead to overutilization or inappropriate utilization.[139] The genetic test alone is not enough to diagnose the disease and only indicates if one of the gene mutations is present.[140] Without a confirmed diagnosis, the Requestor's medications will not be prescribed, and the Requestor has no other financial interest in the disease beyond its two medications.[141] Here, the nexus between the remuneration offered and the ordering of products is attenuated.
2. The program is unlikely to skew clinical decision-making or raise patient safety or quality of care concerns.[142] First, physicians are not incentivized to recommend or prescribe the Requestor's products.[143] Second, patients can benefit from earlier detection, shortening the time between the onset of symptoms and a diagnosis and enabling treatment during the early stages of the disease.[144]
3. The program has safeguards to prevent its use as a marketing or sales tool.[145] The Requestor cannot identify individual patients or physicians from the data shared by the vendors.[146] The sales force cannot access

135. *Id.*
136. *Id.* at 7.
137. *Id.*
138. *Id.*
139. *Id.*
140. *Id.*
141. *Id.* at 7–8.
142. *Id.* at 8.
143. *Id.*
144. *Id.* at 8–9.
145. *Id.* at 9.
146. *Id.*

> any data and does not distribute materials in a personalized manner.[147] The laboratory vendor cannot promote the program to patients or providers. The counseling vendor cannot discuss treatment options or promote the Requestor's medications to patients.[148]

The OIG, through its analysis, held that although the sponsored genetic testing program technically generates prohibited remuneration under the AKS, it would not impose sanctions on the Requestor.[149]

2. OIG Advisory Opinion 24-12 (AO 24-12)

The OIG wrote its second opinion on sponsored genetic testing programs in AO 24-12, two and a half years after AO 22-06. The OIG distinguished AO 24-12 based on the rarity of the genetic condition and the specificity of both the genetic test and the Requestor's medication.

a) Factual Background

The Requestor manufactures one FDA-approved medication that treats an ultra-rare genetic condition (the "condition").[150] Here, the condition leads to recurrent kidney stones and chronic kidney disease that can progress to end-stage renal disease.[151] The condition has three known subtypes, each caused by one type of genetic mutation.[152] The Requestor manufactures one FDA-approved medication that only treats Subtype 1, the most severe and common subtype, affecting approximately 80 percent of patients with the condition.[153]

i) The Genetic Test

The Requestor's sponsored program offers three types of genetic tests, each with varied levels of specificity.[154] The first genetic test is a forty-five-gene panel that tests for multiple genetic disorders associated with kidney stone diseases.[155] The panel largely tests for rare or ultra-rare diseases to rule out potential causes of symptoms rather than to diagnose a specific genetic condition.[156] The second genetic test is condition-specific, testing only for the

147. *Id.*
148. *Id.*
149. *Id.* at 10.
150. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., OIG ADVISORY OPINION NO. 24-12, at 2 (2024) [hereinafter AO 24-12], https://oig.hhs.gov/documents/advisory-opinions/10117/AO-24-12.pdf.
151. *Id.*
152. *Id.*
153. *Id.* at 2–3.
154. *Id.* at 3.
155. *Id.*
156. *Id.*

three subtypes of the genetic mutation.[157] The condition-specific test is appropriate for patients with a family history or as a follow-up to preliminary tests that strongly indicate the condition.[158] The third genetic test is familial variant testing, narrowly testing for a specific variant or mutation seen in a direct relative.[159] All three genetic tests are commercially available by laboratories outside of the sponsored genetic testing program.[160]

The Requestor distinguished how the genetic test compares to other clinical methods used to diagnose the condition. The genetic mutation that causes the condition results in an overproduction and accumulation of oxalate; however, oxalate accumulation can occur in organs other than the kidneys.[161] Thus, the symptoms of recurrent kidney stone disease are non-specific and overlap with other diagnoses.[162] Additionally, the traditional method of testing requires urine collection over a twenty-four-hour period, possibly twice—an inconvenient, costly, and difficult collection method with poor compliance and accuracy.[163] Genetic testing similarly faces limited insurance coverage.[164] The Requestor reflects on these challenges to explain how the condition's diagnosis is often delayed.[165]

A genetic test is not required to prescribe the Requestor's medication to patients.[166] However, the Requestor's medication is only approved to treat Subtype 1 of the condition, and not all patients diagnosed with Subtype 1 are prescribed the medication.[167] Instead, the patient's healthcare provider must determine if the medication is appropriate by considering factors, such as the patient's average oxalate levels, lifestyle and dietary changes, and other competing products and medications.[168]

ii) The Sponsored Program

The Requestor instituted its program intending to use genetic testing as a diagnostic resource to identify, diagnose, and treat inherited diseases, and "particularly, to support disease awareness around hereditary conditions that

157. *Id.*
158. *Id.*
159. *Id.*
160. *Id.*
161. *Id.* at 2.
162. *Id.*
163. *Id.*
164. *Id.* at 3.
165. *Id.* at 2.
166. *Id.* at 3.
167. *Id.*
168. *Id.*

may cause kidney stones."[169] The Requestor entered an arrangement with a contracted laboratory, where the laboratory or a subsidiary furnishes the genetic testing and counseling services.[170] The healthcare provider can order one of the three genetic tests for an eligible patient.[171] The provider can additionally order a sponsored assay test if the initial test results are inconclusive.[172] The Requestor does not receive any identifiable patent data that would allow the determination of a specific patient's genetic test or results.[173] Likewise, the Requestor does not receive information to identify the ordering healthcare providers or their institutions.[174] Two designated individuals—a program lead and a data lead—receive de-identified aggregate data to monitor program efficiency and ensure that the program's contractual and operational obligations are met.[175] Neither individual has any performance objectives or compensation incentives linked to the Requestor's products, including the medication.[176]

iii) Requestor's Marketing

The Requestor offers two websites that provide general disease awareness information about the condition.[177] The first website is mainly directed toward the public (including patients), offering guidance on managing the condition and providing connections to supportive organizations.[178] The public-oriented website includes information about the sponsored genetic testing program but is not branded with the Requestor's medication or specific therapeutic options.[179] The second website is tailored to healthcare professionals, educating them about the condition and genetic testing as a diagnostic tool.[180] The provider-oriented website similarly does not include medication branding or specific therapeutic information.[181] However, the Requestor is identified as the website sponsor "for transparency."[182] Thus, the Requestor's websites aim to educate about the condition and inform the public and healthcare providers

169. *Id.* at 4.
170. *Id.*
171. *Id.* at 5.
172. *Id.*
173. *Id.* at 6.
174. *Id.*
175. *Id.* at 7.
176. *Id.*
177. *Id.* at 4.
178. *Id.*
179. *Id.*
180. *Id.*
181. *Id.*
182. *Id.* at 4 n.5.

about the sponsored genetic testing program—all without advertising the Requestor's medication.

b) OIG Opinion and Holding

The OIG issued AO 24-12 in December 2024, affirming its earlier decision in AO 22-06: the OIG may issue a favorable advisory opinion if a program presents a sufficiently low risk of fraud and abuse.[183] The OIG's rationale in AO 24-12 aligns with the same three rationales in AO 22-06 while supplementing specific facts about the Requestor's sponsored program:

1. The program's safeguards reduce the risk of overutilization or inappropriate utilization.[184] The eligibility criteria are "specific and narrow," limited to patients with impaired renal function or a family history of the condition.[185] Similarly, the condition is ultra-rare, where the tests are narrowly tailored to rule out rare kidney stone diseases rather than diagnose the condition in most cases.[186]
2. The program is unlikely to skew clinical decision-making or raise concerns about patient safety or quality of care.[187] The sponsored tests are already commercially available outside of the program.[188] The Requestor does not incentivize healthcare providers to prescribe its medication, which is only prescribed to treat some—but not all—Subtype 1 patients.[189] Similarly, the Requestor cannot target marketing efforts because it does not receive identifiable patient or provider information.[190]
3. The remuneration provided by the Requestor to the laboratory and subsidiary presents a low risk of fraud and abuse, despite the potential for direct or indirect referrals for the Requestor's medication.[191] The Requestor pays fixed fees for the contracted services and only receives de-identified information.[192] The laboratory and subsidiary only discuss genetic tests and hereditary diseases, not treatment options.[193]

183. *Id.* at 8.
184. *Id.* at 9.
185. *Id.*
186. *Id.*
187. *Id.*
188. *Id.*
189. *Id.*
190. *Id.*
191. *Id.*
192. *Id.*
193. *Id.*

Although the sponsored genetic program resulted in potential remuneration, the OIG determined it would not impose administrative sanctions on the Requestor for AKS violations.[194]

3. Implications

AO 22-06 and AO 24-12 provide guideposts for favorable safeguards and signal a green light for the Requestors to proceed with their sponsored genetic testing programs. Even so, the OIG issues its rulings within strict confines, clarifying that each advisory opinion applies only to the specific Requestor and cannot be relied upon by any other person.[195] Likewise, the opinions are limited to the Requestor's genetic testing program and cannot be applied to any other program.[196] The opinions warn that any differentiation in the facts or a clearer nexus between remuneration and purchases of the Requestor's products would likely result in a different outcome.[197] Lastly, the advisory opinions only apply to the statutory provisions cited in the analysis—the OIG declines to comment on any other regulation or law that could apply to the program.[198]

On balance, AO 24-12 simultaneously narrows and widens the scope of prior AO 22-06. The Requestor in AO 24-12 sponsored a genetic test that diagnoses the genetic disorder without parallel testing, thus narrowing the OIG's inquiry to one test with independent diagnostic abilities. However, the genetic condition in AO 24-12 is ultra-rare and manifests in three subtypes, where the Requestor's medication treats just one subtype.[199] Additionally, the Requestor's medication is not the only available treatment, and healthcare providers must consider other therapeutic options before prescribing it.[200] These elements broaden the analysis, introducing fact-specific considerations that depend on both the genetic test and the condition.

Similarly, it is unclear if AO 24-12 supersedes or coexists with AO 22-06. While the factual differences between the two opinions allow them to coexist, recency could push deference toward AO 24-12. At a minimum, AO 24-12 provides new food for thought on compliance safeguards. For example, AO 22-06 established data protection from marketing use as an implicit compliance requirement. Under AO 24-12, public-facing websites—branded with the Requestor's name for transparency—could become a recommended

194. *Id.* at 10.
195. AO 22-06, *supra* note 106, at 10.
196. *Id.*
197. *Id.* at 8.
198. *Id.* at 10.
199. AO 24-12, *supra* note 150.
200. *Id.* at 3.

feature for sponsored genetic testing programs. Although the OIG's narrowly disclosed opinions stress that they are bespoke to the Requestor's specific program, they nonetheless create pressure for sponsors to adopt similar safeguards.

While pharmaceutical manufacturers can deduce a few clear compliance guidelines from the advisory opinions, they must frame this deduction on two levels: (1) a fine-tuned inquiry on program-specific safeguards, and (2) a wide-cast inquiry on other applicable regulations. Manufacturers must proceed with great caution, understanding that any slight variation could flag their program for remuneration sanctions, not only from the OIG but from any other regulatory bodies as well.

B. AN UNFAVORABLE OUTCOME: *ULTRAGENYX*

The *Ultragenyx* settlement outlines a sponsored genetic testing program that violated the AKS and faced $6 million in sanctions. After paying for genetic test results from a contracted laboratory, the Ultragenyx sales group followed up by marketing directly to ordering physicians. Ultragenyx faced harsh criticism for its conduct, serving as a grave warning to other manufacturer-sponsors.

1. Factual Background

Ultragenyx is a pharmaceutical manufacturer that develops therapies and treatments for rare diseases.[201] For example, Ultragenyx developed and sells Crysvita, a drug that treats X-linked hypophosphatemia (XLH).[202] XLH is a rare, inherited disorder that can lead to soft, weak bones and features such as bowed or bent legs, short stature, and dental abscesses.[203] XLH is characterized by low phosphate levels in the blood, which can be difficult to diagnose or susceptible to confusion with other disorders that have similar symptoms.[204]

a) The Genetic Test

A genetic test is often required to make a definitive diagnosis of XLH.[205] Ultragenyx was aware that, in some instances, physicians required a positive genetic test result to diagnose XLH and prescribe Crysvita to a patient.[206]

201. Settlement Agreement at 1, United States ex rel. Ruggiero v. Ultragenyx Pharm. Inc., No. 1:21-cv-11176-ADB, at 1 (D. Mass. Dec. 19, 2023) [hereinafter Ultragenyx Settlement Agreement], https://www.justice.gov/d9/2023-12/usa_v._ultragenyx_-_settlement_agreement.pdf.

202. *Id.*

203. *Id.*

204. *Id.*

205. *Id.*

206. *Id.* at 2.

Ultragenyx was equally aware that insurers—including Medicare and Medicaid—sometimes require a positive genetic test result for the XLH mutation to reimburse prescriptions of Crysvita.[207] In these cases, the lack of a genetic test was the primary obstacle preventing a Crysvita prescription.

b) The Sponsored Program

Ultragenyx established an agreement with a third-party laboratory to conduct the necessary genetic testing to diagnose XLH and provide the results to the ordering physician.[208] Separately, Ultragenyx paid the laboratory to provide the test results back to Ultragenyx.[209] The test results sent to Ultragenyx did not include patient names but did include the ordering physician's name, along with a de-identified patient ID number, the test order date, and the test result itself (collectively referred to as the "results report").[210]

c) Ultragenyx's Marketing

Ultragenyx shared the laboratory results report with its commercial team, which used the results to identify potential Crysvita patients and their physicians and pursue them with follow-up marketing initiatives.[211] The sales force also followed up with physicians on the test results.[212] This internal practice of receiving and distributing test results to the sales force and instructing Crysvita sales calls to physicians who ordered a test or had patients with positive test results continued until Ultragenyx became aware of AO 22-06 in April 2022.[213]

2. Settlement Agreement Between the DOJ on Behalf of the OIG and Ultragenyx

In December 2023, the DOJ, acting on behalf of the OIG, Ultragenyx, and the Relator, reached a $6 million settlement agreement.[214] Ultragenyx admitted, acknowledged, and accepted responsibility for its conduct from February 1, 2019 through May 30, 2022.[215] Ultragenyx's conduct resulted in the submission of false claims to Medicare and Medicaid by paying remuneration to patients and the laboratory vendor, thereby violating the AKS.[216] For patients,

207. *Id.*
208. *Id.*
209. *Id.* at 2–3.
210. *Id.* at 3.
211. *Id.* at 2–3.
212. *Id.* at 3.
213. *Id.*
214. *Id.* at 1, 3–4.
215. *Id.* at 2–3.
216. *Id.* at 3.

Ultragenyx covered the cost of genetic testing, which could induce the purchase of Crysvita and result in reimbursement under Medicare or Medicaid.[217] For the laboratory vendor, Ultragenyx induced the laboratory to separately provide the results report to Ultragenyx, consequently enabling Ultragenyx's sales force to target physicians to prescribe Crysvita reimbursable through Medicare and Medicaid.[218] These two operations were designed to encourage Crysvita prescriptions and violated the AKS by improperly influencing federal healthcare program billing.

3. Implications

The settlement agreement is brief and direct. In just four pages, the settlement agreement summarizes Ultragenyx's medication, sponsored genetic testing program, conduct, and liability.[219] Ultragenyx admitted and accepted responsibility for AKS violations and paid millions in fines to end the dispute.[220] Still, the full extent of conduct alleged against Ultragenyx is not clear.

From a high-level perspective, Ultragenyx's payment to receive a results report and its sales force's use of the report for targeted follow-ups were irrefutable AKS violations. From a closer view, however, there are potential margins for permissible conduct that are not fully teased out. For example, if Ultragenyx received a results report without the ordering physician's name, the scale might have tipped toward usage for tracking purposes only, thereby reducing sales and marketing concerns.

Likewise, the settlement agreement does not explain the timeline of Ultragenyx's conduct. While Ultragenyx admits it ceased providing results reports to its sales force after learning of AO 22-06 in April 2022, the alleged conduct continued through May 30, 2022.[221] Likewise, the agreement does not outline Ultragenyx's internal plan to restructure its results reports dissemination and reinstruct sales force personnel to stop outreach to physicians. The settlement agreement does away with Ultragenyx's violations and implicitly assumes the company has taken the proper steps to reconcile its internal practices and procedures. However, these ambiguities and slight distinctions become readily apparent when planning future conduct around the settlement agreement holdings.

217. *Id.*
218. *Id.*
219. *See id.* at 1–4.
220. *Id.* at 2.
221. *Id.* at 3.

Lastly, the DOJ represented the United States as a party in the litigation and acted on behalf of the OIG.[222] Following the settlement, the Attorney's Office issued a press release to "[l]et this case be a warning to others," stating that "anyone engaging in similar conduct [would] face similar consequences."[223] The press release targets pharmaceutical manufacturers that "insert themselves" into the physician-patient relationship by potentially undercutting the objectivity of treatment decisions.[224] The DOJ made clear that Ultragenyx "will not be allowed to exploit patient data to target patients for treatments in order to boost their bottom line at the expense of taxpayer-funded health care programs."[225] These harsh, accusatory statements certainly send warnings to pharmaceutical manufacturers to avoid any intervening in clinical decision-making. Yet, for manufacturers trying to avoid intervention while promoting a compliant sponsored genetic testing program, the question still stands: which behaviors are fraudulent or abusive?

C. AN UNCERTAIN FUTURE: SHIFTING REGULATORY REVIEW

In February 2024, the DOJ subpoenaed BioMarin Pharmaceuticals regarding its sponsored genetic testing program for two medications. BioMarin Pharmaceuticals agreed to fully comply with the investigation but also expressed concerns about an industry-wide sentiment: the simultaneous breadth and narrowness of regulation makes compliance an ambiguous concept.

1. An Outstanding DOJ Subpoena of BioMarin Pharmaceuticals

BioMarin Pharmaceuticals is a biotechnology company that develops genetic therapies for conditions with significant unmet medical needs.[226] In February 2024, BioMarin Pharmaceuticals announced that it was subpoenaed by the DOJ to produce documents regarding its sponsored testing programs for two FDA-approved medications, Vimizim and Naglazyme.[227]

222. *Id.* at 1. Note that the OIG is an independent entity within the Department of Justice. *Office of the Inspector General*, U.S. DEP'T OF JUST., https://www.justice.gov/doj/office-inspector-general.

223. Press Release, U.S. Dep't of Just., Pharmaceutical Company Ultragenyx Agrees to Pay $6 Million for Allegedly Paying Kickbacks to Induce Claims for its Drug Crysvita (Dec. 21, 2023) (internal quotations omitted) [hereinafter Ultragenyx Press Release], https://www.justice.gov/usao-ma/pr/pharmaceutical-company-ultragenyx-agrees-pay-6-million-allegedly-paying-kickbacks-induce.

224. *Id.*

225. *Id.*

226. *About Us*, BIOMARIN, https://www.biomarin.com/company/.

227. BioMarin Pharm. Inc., Annual Report 48 (Form 10-K) (Feb. 26, 2024).

In response, BioMarin produced the requested documents and announced full cooperation with the DOJ investigation.[228] However, BioMarin also acknowledged that while it seeks to comply with the AKS, its sponsored testing programs may not meet all the criteria for safe harbor protection.[229] BioMarin highlighted that practices intended to induce prescribing, purchases, or recommendations could be subject to scrutiny.[230] In BioMarin's words, "[t]here is no assurance that such sponsored testing programs . . . will not be found to violate such laws."[231]

The DOJ's findings and next steps in the investigation are still outstanding while BioMarin's sponsored testing programs and medications, each with over a decade of FDA approval, are examined.[232]

2. *Post*-Loper Bright *Risks to Regulatory Agency Authority and Rulemaking*

In June 2024, the Supreme Court overruled *Chevron* in *Loper Bright Enterprises v. Raimondo,* opening a new chapter for the judicial review of agency action.[233] In the context of sponsored genetic testing, agencies face uncertainty in two key areas: authority and rulemaking. First, the FDA's ability to interpret and subsequently regulate medical devices could face increased scrutiny—particularly as the FDA expands oversight to new medical device categories, including LDTs.[234] Second, the FDA and the OIG's rulemaking authority could similarly face more frequent challenges. For example, the OIG's safe harbor provisions are extensions of the AKS that expand protection from prosecution to specifically enumerated arrangements.[235] If a safe harbor provision narrows the requirements for protection, where compliance with the provision necessarily satisfies a broader statutory exemption, courts may still defer to the statutory exception rather than the agency's interpretation.[236] Looking forward, these open areas are susceptible to judicial review and signal the need to consider administrative fallbacks or alternate avenues to impose change. To preserve the FDA and the OIG's ability to regulate and issue

228. *Id.*
229. *Id.*
230. *Id.*
231. *Id.*
232. *See* BioMarin Pharm. Inc., Quarterly Report 55 (Form 10-Q) (June 30, 2024).
233. Loper Bright Enters. v. Raimondo, 603 U.S. 369 (2024).
234. *See* FDA In Vitro Diagnostic Medical Devices, 89 Fed. Reg., *supra* note 37.
235. *See* U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., *supra* note 87.
236. *See id.*

guidance, congressional action will be imperative to delegate and affirm agency rulemaking authority.[237]

3. *Questions Posed for the Genetic Testing Industry, Particularly Regulatory Agencies*

The actively shifting role of regulatory agencies and courts in statutory interpretation and enforcement actions creates ambiguity for the future of sponsored genetic testing programs. BioMarin's briefing to the SEC highlights a key concern recognized by the industry:

> Due to the *breadth* of the healthcare and privacy and data protection laws described above, the *narrowness* of available statutory and regulatory exceptions and safe harbors and the *increased focus* by law enforcement authorities in enforcing such laws, our business activities could be subject to challenge under one or more of such laws.[238]

This statement highlights a critical issue: statutory regulations specific to sponsored testing programs are few and far between, while government agencies aggressively ramp up enforcement efforts.[239] Pharmaceutical manufacturers are caught in a crossfire, where the decision to offer a sponsored testing program that diagnoses patients with genetic disorders instead risks hefty monetary fines. Regulatory agencies must answer key questions for manufacturers to proceed with certainty. First, which agency should have the authority to draft and oversee compliance guidance for sponsored genetic testing programs? Second, which features of sponsored genetic testing programs should be included in compliance guidance?

IV. GAUGING AN APPROPRIATE THRESHOLD FOR REGULATORY OVERSIGHT AND GUIDANCE, AND FORGING A PATH FORWARD TO SPONSORED GENETIC TESTING COMPLIANCE

No single resource comprehensively outlines the compliance standards for sponsored genetic testing programs. Instead, sponsorship and genetic testing are separately overseen by two regulatory agencies: the OIG oversees sponsorship, while the FDA regulates genetic testing.

237. *Loper Bright*, 603 U.S. at 395.

238. Form 10-K, *supra* note 227, at 50 (emphasis added).

239. Enforcement priorities are also susceptible to change between administrations and political appointments, where the HHS Secretary is an elected official.

Sponsored genetic testing programs challenge a niche intersection between the premarket approval of genetic tests and the use of those tests in sponsored programs, where third-party vendors provide them at no cost to physicians or patients. This intersection prompts evaluation of the FDA's and the OIG's roles. Section IV.A calls for cross-agency collaboration between the FDA and OIG to synthesize their distinct roles and determine the appropriate considerations for a compliance guidance document. Section IV.B proposes a risk-based spectrum approach to assess and enforce compliance considerations in sponsored genetic testing programs.

A. REGULATORY AGENCIES MUST MODIFY EXISTING COLLABORATIONS TO JOINTLY DRAFT A COMPLIANCE GUIDANCE

The FDA and the OIG have distinct regulatory motivations in their independent enforcement actions that are not entirely captured by the AKS. However, existing FDA initiatives should be adapted to create guidance and enforcement mechanisms specific to sponsored genetic testing programs.

1. The FDA and the OIG Have Distinct Approaches to Regulating Sponsored Genetic Testing Programs That Cannot Be Reconciled Through the AKS

The FDA and the OIG have entirely separate motivations that inform their regulation of sponsored genetic testing programs. Even so, the OIG maintains auditing power over the FDA and can propose recommendations to the FDA. This existing dynamic is not conducive to AKS regulation, nor does the AKS have any provisions that align with sponsored genetic testing regulation.

a) The FDA Oversees Genetic Test Safety and Reliability While the OIG Oversees Financial Kickbacks

The OIG acts as an oversight committee for the FDA. While the OIG's role naturally implies that it works toward the same outcomes as the FDA, each agency has fundamentally different motives and leadership that shape the focus of its investigations, opinions, and individual regulatory goals.

The FDA ensures the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices.[240] As of January 2024, the FDA oversees over 6,500 medical device products.[241] Medical devices are part of the FDA's medical device and radiological health programs, which had a $746.2 million budget in FY 2023—yet only made up 11 percent of the FDA's

240. *What We Do*, FDA, https://www.fda.gov/about-fda/what-we-do (last updated Nov. 21, 2023).

241. FDA, FDA AT A GLANCE (2024), https://www.fda.gov/media/175664/download.

total budget for the year.[242] While the FDA does manage the substantive function and classification of medical devices, where genetic tests can be considered medical devices, the FDA's regulation of genetic tests is highly variable.[243]

The FDA's official recognition of LDTs as medical devices exemplifies its motivation to ensure the safety and effectiveness of tests increasingly used to make critical healthcare decisions.[244] However, the FDA's efforts to finally regulate LDTs might be taking force too little, too late. Public health concerns have mounted over a decade as LDTs advanced to high-tech instrumentations used in large testing volumes, steadily impacting more and more patients.[245] Evidence from scientific literature, class-action lawsuits, and the FDA's own experience demonstrated that some LDTs provided inaccurate test results or performed worse than FDA-authorized tests.[246] Concurrently, LDTs were used to select cancer treatment, aid in COVID-19 diagnoses, manage rare diseases, and identify patients' risk of cancer.[247] In response, FDA Commissioner Dr. Robert M. Califf announced that the new LDT rule "aims to provide crucial oversight . . . to help ensure that important health care decisions are made based on test results that patients and health care providers can trust."[248] While the LDT rule is just one corner of the FDA's regulation of genetic tests, the FDA foundationally seeks for patients and physicians to "continue to have access to the tests they need while having greater confidence that the tests they rely on are accurate."[249]

Conversely, the OIG serves to improve compliance, implement enforcement actions, and recover misspent funds, subsequently prioritizing review for kickbacks.[250] In fact, the OIG quantifies its annual performance through enumerated enforcement actions: criminal actions against individuals engaged in Medicare and Medicaid-related crimes, civil actions including false claims, unjust enrichment lawsuits, civil monetary penalty settlements, and

242. *Id.*

243. Javitt, *supra* note 30.

244. Press Release, FDA, FDA Takes Action Aimed at Helping to Ensure the Safety and Effectiveness of Laboratory Developed Tests (Apr. 29, 2024), https://www.fda.gov/news-events/press-announcements/fda-takes-action-aimed-helping-ensure-safety-and-effectiveness-laboratory-developed-tests.

245. *Id.*; *see* Angela M. Caliendo & Kimberly E. Hanson, *Point-Counterpoint: The FDA Has a Role in Regulation of Laboratory-Developed Tests*, 54 J. CLINICAL MICROBIOLOGY 829 (2016).

246. FDA Takes Action, FDA, *supra* note 244.

247. *Id.*

248. *Id.*

249. *Id.*

250. FACT SHEET, *supra* note 66.

exclusions from federal healthcare programs.[251] From its outset, the AKS was enacted in response to increasing claims of fraud and Medicare and Medicaid costs, establishing the basis for the OIG's cost-focused investigations.[252] For example, in the *Ultragenyx* press release, OIG Special Agent in Charge Roberto Coviello stated that "[t]he goals of [the OIG's] continued enforcement in this area are to protect the integrity of taxpayer-funded health care programs such as Medicare and Medicaid."[253] Press releases on other genetic testing kickback schemes similarly promote that "[the OIG's] commitment to safeguarding the integrity of the Medicare program remains unwavering."[254] While the OIG is steadfast in its focus on kickback arrangements as an "investigative priority," it pays little regard to the implications of genetic tests themselves.[255]

Thus, the FDA is motivated by ensuring that only safe and reliable medical devices reach the market, while the OIG is motivated by discovering kickbacks to federal healthcare programs. Each agency focuses on different aspects of a sponsored genetic testing program: the test results report and the billing for those reports. Both agencies must weigh in on the proper conduct to fully address the compliance expectations for a pharmaceutical manufacturer or program sponsor.

b) The OIG Exercises Auditing Power Over the FDA but Encourages the FDA to Have Greater Involvement in Enforcement Actions

Each regulatory agency's enforcement actions demonstrate its distinct roles in overseeing sponsored genetic testing programs. The FDA is the primary gatekeeper for genetic tests to reach the marketplace. Once a test is in the marketplace, the FDA is responsible for continually overseeing its approvals and auditing as needed. At this stage, the OIG becomes a secondary gatekeeper by overseeing transactions between manufacturers, physicians, and patients, particularly targeting kickbacks to federal healthcare programs. The OIG can also exercise its power to audit the FDA's effectiveness in overseeing its approvals. Thus, the OIG not only guides the manufacturing industry but

251. HHS OIG 2022 ANNUAL REPORT, *supra* note 56, at 1.

252. Diké-Minor, *supra* note 2, at 109.

253. Ultragenyx Press Release, *supra* note 223.

254. Press Release, U.S. Dep't of Just., Lab Owner Sentenced for $463M Genetic Testing Scheme (Aug. 18, 2023) (internal quotations omitted), https://www.justice.gov/opa/pr/lab-owner-sentenced-463m-genetic-testing-scheme; *see also* Press Release, U.S. Dep't of Just., Doctor and Wife Admit Genetic Testing Kickback and Bribery Scheme (Nov. 22, 2023), https://www.justice.gov/usao-nj/pr/doctor-and-wife-admit-genetic-testing-kickback-and-bribery-scheme.

255. Ultragenyx Press Release, *supra* note 223.

also holds other regulatory agencies accountable to its compliance standards and recommendations.

The OIG has previously criticized the FDA for lacking policies and procedures to respond to consumer complaints, including its failure to investigate a major infant formula supply recall.[256] In June 2024, the OIG audited the FDA to determine if it had taken "prompt, appropriate, and effective action" in response to consumer and whistleblower complaints on powdered infant formula products.[257] The OIG determined that the FDA lacked policies and procedures that appropriately received, escalated, and responded to whistleblower complaints.[258] The OIG found that the FDA took over fifteen months to identify and forward one whistleblower complaint and over four months to escalate another complaint to senior leadership.[259] Likewise, the FDA inaccurately entered data into its complaint system for thirty-seven out of sixty-three consumer complaints.[260] From the thirty-seven complaints entered, thirty-two did not have planned follow-up assignments and six had inaccurate complaint results, such as death or life-threatening injury.[261] Lastly, the FDA lacked guidance on when and how to initiate a mission-critical inspection during public health emergencies.[262] Certainly, the health of over 3.5 million infants, many of whom rely on formula at some point, qualified as a public health emergency.[263]

The OIG subsequently proposed nine recommendations, including implementing policies and procedures to determine when and how to conduct

256. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., NO. A-01-22-01502, THE FOOD AND DRUG ADMINISTRATION'S INSPECTION AND RECALL PROCESS SHOULD BE IMPROVED TO ENSURE THE SAFETY OF THE INFANT FORMULA SUPPLY 1 [hereinafter OIG AUDIT OF FDA INSPECTION AND RECALL REPORT], https://oig.hhs.gov/documents/audit/9908/A-01-22-01502.pdf; *see also* U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., THE FOOD AND DRUG ADMINISTRATION'S INSPECTION AND RECALL PROCESS SHOULD BE IMPROVED TO ENSURE THE SAFETY OF THE INFANT FORMULA SUPPLY (2024), https://oig.hhs.gov/reports/all/2024/the-food-and-drug-administrations-inspection-and-recall-process-should-be-improved-to-ensure-the-safety-of-the-infant-formula-supply/.

257. OIG AUDIT OF FDA INSPECTION AND RECALL REPORT, *supra* note 256, at 1.

258. *Id.* at 9.

259. *Id.* at 9–11.

260. *Id.* at 12.

261. *Id.*

262. *Id.* at 15.

263. *Id.* at 1. The United States House of Representatives Subcommittee on Oversight and Investigations met in May 2022 concerning "Formula Safety and Supply: Protecting the Health of America's Babies." *Protecting the Health of America's Babies: Hearing Before the H. Subcomm. on Oversight and Investigations of the H. Comm. on Energy and Com.*, 117th Cong. (2022) https://www.congress.gov/117/meeting/house/114821/documents/HHRG-117-IF02-Transcript-20220525.pdf.

timely inspections and policies and procedures specific to the FDA's recall authority for infant formula.[264] The FDA concurred with all nine recommendations, though none have been implemented.[265] The infant formula recall provides a clear example of the OIG's authority over the FDA and the FDA's subsequent deference in complying with the OIG's demands.

Undoubtedly, the infant formula recall is not the same type of FDA investigation that would be engaged if complaints arose about the safety or efficacy of a genetic test. Nonetheless, the FDA regulates all subject matters with the overarching goal of protecting public health and safety. Likewise, the OIG can audit any of the FDA's oversight initiatives. If the FDA does not implement an OIG recommendation, it could be listed on a publicly accessible tracker that includes the issuance date, the proposed action, and the status.[266] The infant formula recall is just one recent and relevant illustration of the OIG in action, auditing the FDA's efficacy in enforcing regulatory compliance.

Although the OIG's auditing power over the FDA creates somewhat of a supervisory dynamic, the FDA still independently regulates the compliance of genetic tests as medical devices. The OIG steps in when problems or concerns arise regarding the FDA executing its responsibilities. For example, the OIG's infant formula audit assessed the FDA's policies, procedures, and response time metrics.[267] The analyses looked at the internal processes that facilitated the FDA's response, but not the substantive implications, such as the ramifications posed by contaminated infant formula.[268] The OIG was concerned that the FDA lacked awareness of positive contamination results due to insufficient reporting requirements, but it did not further probe the direct health risk to susceptible infants.[269] While both concerns are fundamental in ensuring a compliant infant formula supply, the OIG leans toward the procedural side of FDA operations. Thus, the working relationship between the FDA and the OIG, particularly the OIG's recommendations to the FDA, should be leveraged to address procedural and substantive concerns in sponsored genetic testing programs.

264. OIG AUDIT OF FDA INSPECTION AND RECALL REPORT, *supra* note 256, at 20–21.

265. *Id.* at 53–60; U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., THE FOOD AND DRUG ADMINISTRATION'S INSPECTION AND RECALL PROCESS SHOULD BE IMPROVED TO ENSURE THE SAFETY OF THE INFANT FORMULA SUPPLY (2024), https://oig.hhs.gov/documents/audit/9908/A-01-22-01502.pdf.

266. *See Recommendations Tracker*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., https://oig.hhs.gov/reports/recommendations/tracker/?view-mode=top-unimp-recs&responsible-agency=all#results.

267. OIG AUDIT OF FDA INSPECTION AND RECALL REPORT, *supra* note 256, at 8.

268. *See id.*

269. *Id.* at 19.

The OIG seemingly favors the FDA exercising increased authority in enforcement actions. In 2022, the OIG recommended that the FDA seek legislative authority to enforce FDA assessment plans and impose civil monetary penalties on companies that fail to comply with registration requirements.[270] While the OIG has the leeway to propose idealistic recommendations, implementing them is a separate feat—which may explain why the recommendation has remained outstanding since 2012.[271] Granting the FDA increased authority to enforce a requirement that it already oversees is not outlandish. However, the FDA has long faced resource constraints, particularly in drug and device regulation.[272] In 2002, Congress rescinded and reallocated $71 million in drug safety funding.[273] Currently, the FDA's new LDT rule faces concerns about the FDA lacking the infrastructure to support the review process.[274] While the FDA cannot comfortably take on additional authority with its current resources, it remains the agency that is exceedingly familiar with the dynamics of the medical device industry based on its leadership of the premarket approval process.[275] Therefore, the FDA should not be entirely excluded from enforcement and remuneration concerns; rather, the FDA should instead be invited to assess the appropriate compliance regime. The FDA's ongoing efforts to formalize genetic testing regulation provide valuable insight into regulatory considerations for the review of sponsored genetic testing programs.[276] Establishing a cross-agency initiative would facilitate the development of comprehensive compliance guidance for such programs.

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270. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., OIG'S TOP UNIMPLEMENTED RECOMMENDATIONS: SOLUTION TO REDUCE FRAUD, WASTE, AND ABUSE IN HHS PROGRAMS 41–42 (2022), https://oig.hhs.gov/documents/top-unimp-recs/1206/OIG-TUR-2022-Complete%20Report.pdf. Note that OIG recommended that the FDA seek the civil monetary penalty authority for food facilities. The FDA previously expressed support for the recommendation and its openness to pursuing the authority in the future. *See, e.g.*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., OEI-01-11-00211, DIETARY SUPPLEMENTS: COMPANIES MAY BE DIFFICULT TO LOCATE IN AN EMERGENCY 12 (2012), https://oig.hhs.gov/oei/reports/oei-01-11-00211.pdf.

271. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., OIG'S TOP UNIMPLEMENTED RECOMMENDATIONS, *supra* note 270.

272. *See* INST. MED. F. ON DRUG DISCOVERY, DEV., & TRANSLATION, CHALLENGES FOR THE FDA: THE FUTURE OF DRUG SAFETY, WORKSHOP SUMMARY (2007).

273. *Id.*

274. Melissa B. Miller, Mary Lee Watts & Linoj Samuel, Commentary, *FDA's Proposed Rule for the Regulation of Laboratory-Developed Tests*, 62 J. CLINICAL MICROBIOLOGY (2024).

275. *See supra* Section II.B.2.

276. *See supra* Section II.B.2

c) AKS Safe Harbors are an Improper Statutory Mechanism to Implement Sponsored Genetic Test Guidance That Includes Safety and Reliability Concerns

Safe harbors provide a protective outlet for practices that might otherwise raise suspicion or pose risks of kickbacks but are not treated as offenses.[277] However, obtaining safe harbor protection requires strict compliance with the conditions enumerated in the corresponding safe harbor provision.[278] Currently, no existing safe harbor covers sponsored genetic testing programs directly. The closest potentially relevant safe harbor pertains to discounts, yet the provision precludes induced purchases reimbursed by federal healthcare programs from protection.[279] The safe harbor for discounts specifically excludes from the definition of "discount":

> Supplying one good or service without charge or at a reduced charge to induce the purchase of a different good or service, unless the goods and services are reimbursed by the same Federal health care program using the same methodology and the reduced charge is fully disclosed to the Federal health care program and accurately reflected where appropriate, and as appropriate, to the reimbursement methodology.[280]

Thus, a free genetic test offered in exchange for a future prescription of the same pharmaceutical manufacturer's treatment drug is excluded from the safe harbor provision for discounts. Likewise, AO 22-06, AO 24-12, and the *Ultragenyx* settlement did not consider any safe harbor exemptions in their analyses of each program.[281]

A new safe harbor protection would provide the most immediate and readily enforceable solution, consistent with the OIG's practice over the last thirty years. However, another safe harbor protection would simply revert to the OIG to draft additional features required for compliance. Additionally, relying on safe harbor protections creates a practice of excusing liability for kickbacks and fails to address the larger concern of lacking current guidance for pharmaceutical companies to devise compliant sponsored programs. Physicians and patients are still involved parties interested in receiving valid

277. *Safe Harbor Regulations*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., *supra* note 87.

278. OIG Compliance Program Guidance for Pharmaceutical Manufacturers, *supra* note 94, at 23734.

279. 42 C.F.R. § 1001.952(h).

280. 42 C.F.R. § 1001.952(h)(5)(ii).

281. AO 22-06, *supra* note 106; AO 24-12, *supra* note 150; Ultragenyx Settlement Agreement, *supra* note 201.

test results with lesser concern for marketing tactics or billing practices aimed at federal healthcare programs.

The unfitting OIG-authored safe harbors, coupled with the FDA's and OIG's conflicting motives and enforcement actions, underscores the pressing need for a clearly designated agency to author and lead compliance guidance.

2. Current FDA-Initiated Cross-Agency Collaborations Should Be Adapted for Drafting Sponsored Genetic Testing Program Guidance

The FDA has two existing initiatives that could be jointly revised to address regulatory concerns in sponsored genetic testing program contexts. First, the Collaborative Community Initiative should form a working group to gather industry feedback on sponsored genetic testing program concerns. Second, the Pharmaceutical Fraud Program should serve as a baseline for developing an enforcement program that investigates sponsored genetic testing programs.

a) The FDA Collaborative Community Initiative Should Facilitate a Dialogue Between Pharmaceutical Manufacturers, Regulatory Agencies, and Healthcare Stakeholders

The Collaborative Community Initiative unites public and private sector organizations and individuals to solve shared problems in a collegial setting.[282] Each entity faces individual challenges that underlie a greater vested interest in achieving the best patient outcomes through compliant means.[283]

Here, a collaborative community for sponsored genetic testing programs is needed. These programs are divided between multiple engaged stakeholders: the sponsorship-concerned OIG, the genetic testing-concerned FDA, physicians, patients, pharmaceutical manufacturers, and third-party vendors. Each stakeholder provides a unique perspective and expertise as each party is involved in some facet of a sponsored genetic testing program. A pharmaceutical manufacturer would chair the community, with the FDA and OIG as participants. Other pharmaceutical manufacturers, physicians, and patients would be invited to join. One collaborative community is appropriate to encompass all sponsored genetic testing programs since the stakeholders likely face the same regulations and obstacles. This advantageous and efficient forum would be an opportunity to discuss potential AKS violations without facing liability or the pressures of an audit. The community would be a practical platform for manufacturers and regulatory agencies to openly grapple with their concerns and cooperate to reach an amicable solution.

282. *Collaborative Communities: Addressing Health Care Challenges Together*, FDA, *supra* note 42.
283. *See id.*

To be effective, regulatory agencies must first welcome communication and establish an environment where participants feel safe and open to candidly express their views. Next, the agencies must identify the chief concerns of stakeholders and compare them to the existing regulations or statutes they enforce. By evaluating consistencies and discrepancies between stakeholder concerns and existing regulations, agencies are best placed to address these concerns. They may draft amendments to existing regulations or provide individual feedback to the stakeholders on how to proceed. The agencies may also identify a compliant program and share it as a baseline example for stakeholders, similar to the Case for Quality initiative. In other words, an AO 22-06-like document could be developed into a guidance resource that pharmaceutical manufacturers could faithfully rely upon when structuring sponsored genetic testing programs.

The Collaborative Community initiative is a starting point to invite feedback from the OIG, the FDA, and healthcare stakeholders to share insights, concerns, and lessons learned from prior AKS violations. The collective feedback should be synthesized to propose a new, comprehensive pharmaceutical manufacturer-specific compliance guidance document that incorporates successful Case for Quality-style examples.

b) The FDA Pharmaceutical Fraud Program (PFP) is a Pertinent Criminal Investigation Model That Can Be Adapted to Enforce Healthcare-Specific Violations

The Pharmaceutical Fraud Program (PFP) enables the FDA to prosecute fraudulent conduct and stop public harm caused by medical products that reach the marketplace without proper approval.[284] The PFP partially functions as an enforcement mechanism for sponsored genetic testing compliance.[285] Violations of the AKS are criminal conduct and therefore within the scope of the PFP.[286] However, the variation in FDA regulation of genetic tests means that only some genetic tests would be recognized as "potentially dangerous medical products" or subject to PFP scrutiny.[287] For instance, under the 510(k) and De Novo pathways and the new LDT rule, certain genetic tests that failed to acquire premarket notification or reached the market before the LDT rule are potentially dangerous. The uneven application of PFP poses administrative

284. BOOZANG ET AL., *supra* note 56, at 25; HHS OIG 2022 ANNUAL REPORT, *supra* note 56, at 101.

285. HHS OIG 2022 ANNUAL REPORT, *supra* note 56, at 101.

286. *See id.* ("The PFP is designed to detect, prosecute, and prevent pharmaceutical, biologic, and medical device fraud.").

287. *See id.*

challenges regarding how routinely sponsored genetic testing programs would be investigated.

The PFP satisfies the need for a mechanism that evaluates a product from its earliest development stages while concurrently considering its involvement in fraudulent marketing schemes. However, the extremely high bar to qualify for the PFP and the lengthiness of its investigations are ill-fitted for the comparatively narrower scope of a sponsored genetic testing program. Instead, the FDA and OIG should jointly perform a more limited investigation, focusing on a single pharmaceutical manufacturer. At a minimum, the structural framework of the PFP can serve as a model for a healthcare-focused program targeting criminal violations.

After the Collaborative Community establishes a communication channel to collect feedback from the FDA, OIG, and stakeholders, the PFP offers the most closely aligned framework with the proposed goal of merging medical device oversight and marketing practice review under one agency. The dynamics of the PFP should be leveraged to outline an enforcement program that conducts investigations of sponsored genetic test programs in a feasible, administrable manner.

B. A Risk-Based Spectrum Approach Should Establish Compliance Factors for Sponsored Genetic Testing Programs

The OIG Risk Spectrum is a powerful tool to evaluate fraudulent use of federal healthcare programs. Thus, the Risk Spectrum should be tailored to sponsored genetic testing programs by incorporating program-specific considerations into its existing set of factors. This revision would successfully formulate compliance guidance that does not generate policy concerns.

1. The OIG Risk Spectrum Should be Adapted to Sponsored Genetic Testing Programs by Expanding Upon the Existing Factors with Fact-Specific Considerations

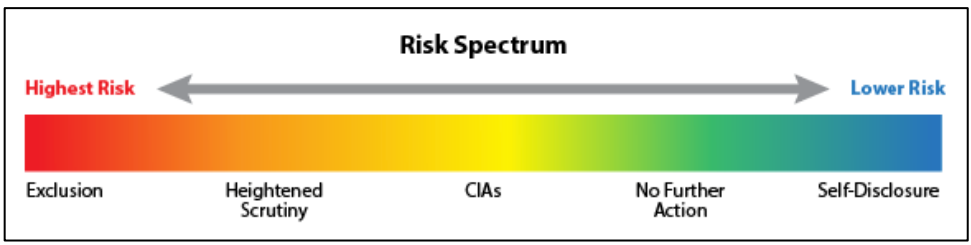
Once established, the joint FDA-OIG task force should first outline the features of a compliant sponsored genetic testing program by drawing on precedent guidance and cases, namely OIG Advisory Opinions and the *Ultragenyx* settlement.

a) The OIG Risk Spectrum Performs a Weighted Assessment That Can Exclude AKS Violators from Participating in Federal Healthcare Programs

The OIG has already established a "Risk Spectrum" tool that provides approaches for resolving healthcare fraud cases under the False Claims Act.[288] Under the AKS, the OIG can exclude entities engaged in fraud, kickbacks, and other prohibited conduct from participating in federal healthcare programs.[289]

Exclusion is an aggressive remedial action that precludes an entity from offering a product or service to anyone who could bill federal healthcare programs.[290] In April 2016, the OIG issued criteria for applying its exclusion authority, which assumes a presumption in favor of exclusion that is rebuttable based on nonbinding factors.[291] While these criteria were established to protect federal healthcare programs, the OIG recognizes that, in practice, compliance must be corrected and strengthened to prevent future violations.[292] The OIG thus debuted a continuum to apply exclusion based on the assessment of future risk to federal healthcare programs:

Figure 1: OIG Risk Spectrum[293]



The OIG concluded that exclusion is not often necessary if the entity agrees to "integrity obligations."[294] Further, the OIG may require corporate integrity agreements in exchange for releasing the exclusion authority.[295] Integrity obligations allow an entity to develop its compliance program while

288. *Fraud Risk and Heightened Scrutiny*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., https://oig.hhs.gov/fraud/fraud-risk-spectrum/.

289. Social Security Act § 1128(b)(7), 42 U.S.C. § 1320(a)–(b)(7).

290. *See* Social Security Act § 1128(b)(7).

291. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., CRITERIA FOR IMPLEMENTING SECTION 1128(B)(7) EXCLUSION AUTHORITY 1 (2016), https://oig.hhs.gov/exclusions/files/1128b7exclusion-criteria.pdf.

292. *Id.* at 2.

293. *Fraud Risk and Heightened Scrutiny*, U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., *supra* note 288.

294. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., *supra* note 291, at 2.

295. *Id.* at 1.

enabling the OIG to oversee and mitigate risks.[296] In other cases, an entity may have a relatively low risk where exclusion or integrity obligations are unnecessary. However, the release of exclusion without integrity obligations is limited to scenarios where there is no egregious misconduct, low financial harm, or where the entity is a successor owner.[297] Likewise, a good-faith self-disclosure of fraudulent conduct or an agreement to robust integrity obligations with a state or the DOJ can be sufficient remedies that do not require exclusion.[298] The OIG's weighted assessment of integrity obligations and surrounding circumstances forms the foundation of the Risk Spectrum.

The entity's placement on the Risk Spectrum depends on a fact-specific inquiry of four factors, each categorized as higher risk, lower risk, or neutral risk.[299] The factors are (1) nature and circumstances of conduct, (2) conduct during investigation, (3) significant ameliorative efforts, and (4) history of compliance.[300] Each factor has a list of considerations that indicate the corresponding risk level, if applicable.[301]

b) The OIG Risk Spectrum Factors Should Incorporate Sponsored Genetic Testing Program-Specific Considerations to Create a Pharmaceutical Manufacturer Risk Spectrum

The OIG's Risk Spectrum has served the OIG in investigating fraudulent violations and assigning exclusionary remedies since 2016.[302] However, the OIG Compliance Program Guidance for Pharmaceutical Manufacturers was issued in 2003.[303] Thus, the Risk Spectrum should form the basis of new manufacturer-oriented guidance outlining compliance risks that can be mitigated at the outset of a sponsored genetic testing program. By directing a risk spectrum to manufacturers, the OIG can define concrete compliance objectives with minimal ambiguity. In turn, the OIG can cite these factors in its investigations as industry-wide benchmarks familiar to both the agency and manufacturers.

In drafting a new "Pharmaceutical Manufacturer Risk Spectrum," the probing questions in the 2003 Compliance Guidance should be integrated into the four OIG Risk Spectrum factors. The Pharmaceutical Manufacturer Risk

296. *Id.* at 2.
297. *Id.* at 2–3.
298. *Id.* at 3.
299. *Id.* at 3–4.
300. *Id.* at 4–7.
301. *Id.*
302. *Id.* at 1.
303. OIG Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg., *supra* note 94.

Spectrum should supplement the risk spectrum factors with considerations specific to sponsored genetic testing programs. These program-specific considerations will frame a fact-specific inquiry for the OIG and manufacturers to use when determining the level of risk to healthcare programs. A particular focus on the "nature and circumstances of conduct" and "significant ameliorative efforts" factors is most appropriate.

i) Nature and Circumstances of Conduct Should Consider the Severity of the Genetic Disorder, the Cost to Administer the Test, and Data Management

Adverse impact on individuals is one of the primary conduct considerations, particularly conduct with the potential to cause any adverse physical, mental, or financial impact to program beneficiaries, recipients, or other patients.[304] However, the adverse impact consideration excludes a lack of patient harm from the risk assessment.[305] For sponsored genetic testing programs, the potential for patient harm from a genetic test is negligible compared to the enduring harm of an undiagnosed genetic disorder. For example, if a genetic test screened for terminal disease with a highly abbreviated life expectancy, the adverse impact of barring a sponsored program would be gravely detrimental to patient outcomes. The severity of the genetic disorder coincides with the value of the genetic test, and the added value of a sponsored diagnosis places a low risk of abuse of federal healthcare programs.

Financial loss to federal healthcare programs is another critical conduct consideration, where a greater amount of actual or intended loss is associated with higher risk.[306] For sponsored genetic testing programs, the administrative costs vary, depending on the target population of the genetic disorder. In AO 22-06, the permissible program did not standardize the distribution of test kits, and physicians could order additional kits from the testing vendor as needed.[307] Physicians were therefore active parties in using additional test kits that could, in turn, bill federal healthcare programs. Correspondingly, the physician's specialty influences the patient population served. For example, cardiology, immunology, and neurology are vastly different practice areas with vastly different genetic disorders. If the symptoms of a neurological disorder predominantly present in patients sixty-five years and older, physicians will

304. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., *supra* note 291, at 4.

305. *Id.*

306. *Id.*

307. AO 22-06, *supra* note 106, at 6.

administer diagnostic genetic tests to Medicare-qualifying individuals, subsequently increasing the cost to federal healthcare programs. Thus, testing frequency is beyond the control of the manufacturer or program sponsor, and the underlying genetic disorder complicates quantifying actual or intended loss costs.

Financial implications can also be evaluated by the diagnostic capability of the genetic test and its impact on medication prescriptions. In AO 22-06, the Requestor's genetic test could not independently diagnose the disorder.[308] In this regard, the genetic test was unnecessary if a different test could independently diagnose the disorder. However, the Requestor's genetic test added value by identifying which form of the genetic mutation was present.[309] Identifying the specific genetic mutation form was inherently valuable for understanding symptoms, such as earlier disease progression in the hereditary form.[310] Again, however, the genetic test might not be necessary if the Requestor's treatment options do not differentiate between mutation forms. In AO 22-06, the Requestor manufactured two medications that treated both mutation forms.[311] Here, if the goal was to prescribe the Requestor's medications, then the genetic test results served a marginal role in confirming which medication was appropriate. Instead, the mutation form results were more informative in anticipating disease progression and establishing a monitoring plan for asymptomatic patients with a genetic mutation. The OIG analogously determined that the risk of fraud and abuse was sufficiently low in AO 22-06.[312] Improved patient information and testing as a diagnostic supplement are proposed Risk Spectrum factors that pose a low risk for federal healthcare kickbacks. While financial losses remain a key motivator for OIG enforcement under the AKS, they should carry less weight in sponsored genetic testing program contexts because the diagnostic value of the tests outweighs the risk of fraud and abuse.

Conduct that occurs as part of a pattern of wrongdoing and conduct that continues until or after the person learns of a government investigation are both high-risk considerations.[313] In *Ultragenyx*, the company's distribution of genetic test results reports to sales force personnel represented a pattern of wrongdoing that persisted until Ultragenyx learned of AO 22-06 and halted

308. *Id.* at 2.
309. *Id.* at 2–3.
310. *Id.*
311. *Id.* at 2.
312. *Id.* at 7.
313. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., *supra* note 291, at 4.

the practice.[314] The *Ultragenyx* situation is uniquely situated between two conduct considerations. On one hand, Ultragenyx wrongfully acquired results reports through a separate payment to the third-party laboratory. Likewise, Ultragenyx is not shielded by any safe harbors: sharing information with sales personnel does not qualify for personal services or employment safe harbors because the remuneration is to the physicians prescribing Ultragenyx medications, not the sales personnel.[315] On the other hand, Ultragenyx complied with de-identification standards by acquiring results reports that removed patient names and corresponding health information.[316] There is no explicit requirement that physician names must also be removed. While Ultragenyx might have had "actual knowledge" that the results report information could be used to identify patients, they only contacted the physician regarding the test results.[317] Ultragenyx's practices tread a fine line between leveraging patient data for marketing treatments and avoiding outrightly using patient names. The results reports were at the heart of the *Ultragenyx* case and certainly motivated the DOJ in its attack on Ultragenyx's conduct. From an AKS standpoint, regardless of how Ultragenyx managed the results reports, the end goal of marketing Crysvita was achieved.

Ultragenyx did stop its activity as soon as it learned of AO 22-06.[318] While this act could be construed as an admission of fault, Ultragenyx simultaneously took accountability to remedy its data management practices. Ultragenyx's underlying motivations are cloudy, but its external conduct, according to the OIG Risk Spectrum, carries less risk. Of course, this conduct did not stop the DOJ from reaching a $6 million settlement with Ultragenyx.[319] Thus, conduct that continues following a federal investigation is a reduced concern compared to other conduct considerations. For sponsored genetic testing programs, *Ultragenyx* teaches a daunting lesson for marketing data management. Moving forward, pharmaceutical manufacturers are likely to keep results reports under lock and key. While patterned or continuous conduct merits scrutiny, it should take deference to adverse impact and financial motivation considerations.

314. Ultragenyx Settlement Agreement, *supra* note 201, at 3.
315. *Id.*
316. *Id.*; 42 C.F.R. § 164.514(b)(2).
317. Ultragenyx Settlement Agreement, *supra* note 201, at 3; 42 C.F.R. § 164.514(b)(2)(ii).
318. Ultragenyx Settlement Agreement, *supra* note 201, at 3.
319. *Id.* at 2–3.

ii) Significant Ameliorative Efforts Should Consider Alternate Treatment Availability and Supplementary Informational Materials

Significant changes within an entity are a primary consideration in evaluating ameliorative efforts.[320] If the entity is a pharmaceutical manufacturer, then the *Ultragenyx* marketing data management concerns arise again. If a pharmaceutical manufacturer takes disciplinary action or devotes additional resources to remedy or enforce compliance, there is a lower risk to federal healthcare programs. These considerations align with the existing OIG Risk Spectrum.[321] If the entity includes the physician and patient, then the mechanisms of the sponsored genetic testing program warrant closer review.

The availability of alternate treatments increases the risk associated with sponsorship programs. If a program sponsor manufactures a treatment for the genetic disorder diagnosed in the sponsored genetic test, then an inevitable motivation to attain subsequent prescriptions exists. Alternate treatment options compete with the program sponsor or manufacturer, each seeking to acquire as many prescriptions as possible. Treatment options can range from drugs to regenerative therapies to surgeries—each option places a weighty decision on the patient and impacts the treatment plan. Some patients might be better suited to take medications, while others might undergo surgical procedures to treat their symptoms. Regardless, the treatment plan is an intimate, subjective decision between the patient and the physician. Regulatory parties should not interfere unless safety or efficacy concerns arise. Pharmaceutical manufacturers that support patients in achieving the best health outcomes and provide unbiased informational guides to educate patients on their options are the most favorably viewed. Thus, a manufacturer that devotes significant resources to compliance has made significant ameliorative changes.[322]

In AO 24-12, the Requestor required the provider to consider other competing products and medications before prescribing the Requestor's medication.[323] The Requestor also maintained two educational websites—one for patients and one for providers—to further quell competitive conduct concerns.[324] A double-blinded arrangement between the physician and program sponsor that provides a comprehensive account of treatment options,

320. U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., *supra* note 291, at 6–7.

321. *See id.*

322. *Id.*

323. AO 24-12, *supra* note 150, at 3.

324. *Id.*

including lists of manufacturers offering the same medication or different treatment options, would similarly neutralize the risk of fraud or abuse.

Conversely, if no alternatives are available, the physician would prescribe the sponsor's treatment to positive-testing patients, irrespective of whether the patient participated in the sponsored program. In such cases, the sponsored genetic testing program poses a nominal risk since market competition is not a motivating factor for the sponsor or manufacturer. Thus, while alternate treatment options carry high risk, offering patient and physician informational materials and lacking market competition present low risks to federal healthcare programs.

The expected value in patient care greatly outweighs the remuneration or kickback risks in many conduct and ameliorative effort considerations. Thus, the OIG Risk Spectrum criteria must be tailored to integrate sponsored program-specific information and substantive medical considerations. Genetic tests are a powerful tool that present unique regulatory concerns balanced against benefits to regulatory agencies, manufacturers, physicians, and patients. Their innovative potential should be harnessed into a methodical evaluation along a familiar risk-based spectrum.

2. The Proposed Pharmaceutical Manufacturer Risk Spectrum Approach Achieves the Desired Compliance Guidance Form and Does Not Create Policy Concerns

The proposed Pharmaceutical Manufacturer Risk Spectrum refines the existing OIG Risk Spectrum into a sponsored genetic testing program-specific approach while staying consistent with the AO 22-06, AO 24-12, and *Ultragenyx* holdings. In turn, this approach is inclusive of stakeholders in sponsored genetic testing programs and, more broadly, the healthcare industry.

a) The Spectrum Approach Reaches the Same Outcomes in AO 22-06, AO 24-12, and *Ultragenyx*

While the spectrum approach provides tailored guidance to pharmaceutical manufacturers and refines existing considerations for sponsored genetic test programs, its implementation poses administrative challenges. The spectrum approach is a qualitative balancing test. While the focus has been narrowed to a niche sector of the healthcare industry, the programs offered within this sector are still highly variable. Differences exist in genetic disorders, diagnostic capabilities of the tests, and available treatment options. Likewise, each disorder impacts diverse patient populations that may interface with the different offerings of federal healthcare programs. These substantive considerations vary case by case and are subject to the contours of a given

sponsored program. The spectrum approach establishes a middle ground between the two cases.

In AO 22-06, the OIG focused primarily on achieving a definitive diagnosis, prescribing treatment, and establishing safeguards against marketing use.[325] Under the spectrum approach, the genetic test could not independently diagnose the disorder, but its diagnosis of the mutation form (hereditary or spontaneous) made the patient better placed to monitor disease progression.[326] Likewise, the Requestor only used the results report to track participation and entirely avoided marketing.[327] There was an adequately low risk across all factors to be considered compliant and not federal healthcare program abuse.

In AO 24-12, the OIG focused primarily on the rarity of the genetic disorder and the narrow applications of both the genetic test and medication.[328] Under the spectrum approach, the provider exercised discretion in selecting from three genetic test options.[329] The provider only prescribed the Requestor's medication after evaluating competitor treatments.[330] The Requestor also provided informative websites where the online information and branding—despite listing the Requestor's name for transparency—dually strengthened the program's credibility.[331] Lastly, existing diagnostic options delayed results and lacked adequate insurance coverage.[332] The Requestor's consideration of alternatives and disclosure to the OIG created a low risk for fraud and abuse that would satisfy spectrum compliance.

In *Ultragenyx*, the OIG was most concerned with data management.[333] Under the spectrum approach, the patient data complied with de-identification results.[334] Similarly, Ultragenyx undertook remedial efforts to stop high-risk conduct upon learning of the AO 22-06 decision.[335] However, its practice of targeting positive-testing patients through their ordering physicians demonstrated gamesmanship and interfered with physician-patient decision-making.[336] A double-blinded program would have minimized the significant risk of abuse. The spectrum approach would have reached the same outcome

325. *See generally* AO 22-06, *supra* note 106.
326. *Id.* at 2.
327. *Id.* at 5.
328. *See generally* AO 24-12, *supra* note 150.
329. *Id.* at 5.
330. *Id.* at 3.
331. *Id.* at 4 n.5.
332. *Id.* at 2–3.
333. *See generally* Ultragenyx Settlement Agreement, *supra* note 201.
334. *Id.* at 3.
335. *Id.*
336. *See id.*

as in *Ultragenyx*, but with less hostility than the DOJ or with lower remuneration sanctions.

The spectrum approach is a promising avenue to reform sponsored genetic testing program investigations, but its adoption depends on administrative and substantive implementation by the OIG and FDA, respectively. In turn, regulatory reform would better equip pharmaceutical manufacturers to gauge and improve the compliance of their sponsored genetic testing programs.

b) The Spectrum Approach Accounts for Stakeholder Interests within the Larger Healthcare System

Healthcare is a team sport where the key players are patients, providers, and regulatory agencies. Pharmaceutical manufacturers and laboratories are sideline players who support these players when needed.

Patients want timely, accurate diagnoses and treatments to live healthy and fulfilled lives. Understanding that patient safety is the top priority, there are coinciding risks to data privacy.[337] While HIPAA, additional statutes, and certain healthcare practices shield patients, the reality is that a competitive marketplace of vying manufacturers underlies every healthcare transaction.[338] Even so, healthcare is an omnipresent, integral part of everyday life, from taking daily medications to being inundated by pharmaceutical advertisements. The spectrum approach recognizes data management as an independent consideration in its analysis and rewards efforts to safeguard risks to patients in favor of compliance.

Healthcare providers want to practice medicine while being fully informed of current treatment options and alternatives. However, the AKS applies to remuneration received by providers, too.[339] Several other statutes, including the Stark Law, also enumerate expected conduct for physicians in medical decision-making. [340] Thus, physicians can be held personally liable for prescribing test sponsor medications. While the proposed spectrum approach is geared toward pharmaceutical manufacturers, establishing compliance at the outset of a sponsored genetic testing program provides some security to participating physicians. The data management consideration within the

337. *See generally* CHRISTINA MUNNS & SUBHAJIT BASU, PRIVACY AND HEALTHCARE DATA: 'CHOICE OF CONTROL' TO 'CHOICE' AND 'CONTROL' (2017).

338. *See* 110 Stat. 1936; *Understanding Patient Safety Confidentiality*, U.S. DEP'T OF HEALTH & HUM. SERVS., https://www.hhs.gov/hipaa/for-professionals/patient-safety/index.html (last updated Oct. 22, 2024).

339. *See* U.S. DEP'T OF HEALTH & HUM. SERVS., OFF. OF INSPECTOR GEN., *supra* note 71.

340. *See* 42 U.S.C. § 1395nn.

spectrum approach explicitly warns manufacturers against potential marketing outreach or targeting of ordering physicians.

Protecting the private patient-physician relationship is the crux of quality care. Sponsored genetic testing programs should be structured in line with this foundational value. Sponsored programs can respect the patient-physician relationship by providing alternate options supra• and comprehensive education opportunities for physicians and patients alike to make fully informed treatment decisions. By leaving full decisional authority in the hands of the patient and their physician, the spectrum approach ensures that genetic testing is just one step in a patient's care journey, rather than a tool for steering prescriptions.

V. CONCLUSION

While the Advisory Opinions and *Ultragenyx* decisions represent two opposite poles of regulatory compliance, concentrating on the objectives of sponsored genetic testing programs reveals a niche intersection between FDA and OIG oversight. The FDA's primary focus on the safety and efficacy of medical devices is addressed through premarket notification. The OIG's primary focus on fraud or abuse of federal healthcare programs through remuneration is later enforced through the AKS. Sponsored genetic testing programs must carefully navigate the challenge of offering vetted genetic tests at no cost to patients or physicians without kickbacks that run afoul of federal healthcare laws. Pharmaceutical manufacturers must strike this balance by reflecting on AO 22-06 and AO 24-12, which guardedly permitted tests with narrow diagnostic abilities and strict data access restrictions, and *Ultragenyx*, which emphatically denounced the usage of test results for any marketing purposes.

Between these two extremes, the FDA has several community initiatives that welcome stakeholder collaboration, and the OIG has pharmaceutical manufacturer-specific guidance (most recently in 2003). By uniting the FDA and OIG as joint authorities over sponsored genetic testing programs, a risk-based spectrum approach can be formulated to weigh the substantive factors of both genetic tests and sponsored programs. Empowering pharmaceutical manufacturers to self-assess and advance compliance initiatives through a dedicated framework will reduce the sizeable fraud and abuse kickbacks affecting federal healthcare programs and the number of enforcement actions by regulatory agencies.