DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE OF INSPECTOR GENERAL
WASHINGTON, DC 20201

[*We redact certain identifying information and certain potentially privileged, confidential, or proprietary information, unless otherwise approved by the requestor(s).*]

Issued: June 12, 2024

Posted: June 17, 2024

[Address block redacted]

Re: OIG Advisory Opinion No. 24-03 (Favorable)

Dear [redacted]:

The Office of Inspector General ("OIG") is writing in response to your request for an advisory opinion on behalf of [redacted] ("Requestor"), regarding assistance for certain travel, lodging, meals, and associated expenses for qualifying patients receiving [redacted] (the "Product"), a gene therapy product manufactured by Requestor (the "Arrangement"). Specifically, you have inquired whether the Arrangement constitutes grounds for the imposition of sanctions under: the civil monetary penalty provision at section 1128A(a)(7) of the Social Security Act (the "Act"), as that section relates to the commission of acts described in section 1128B(b) of the Act (the "Federal anti-kickback statute"); the civil monetary penalty provision prohibiting inducements to beneficiaries, section 1128A(a)(5) of the Act (the "Beneficiary Inducements CMP"); or the exclusion authority at section 1128(b)(7) of the Act, as that section relates to the commission of acts described in the Federal anti-kickback statute and the Beneficiary Inducements CMP.

Requestor has certified that all of the information provided in the request, including all supplemental submissions, is true and correct and constitutes a complete description of the relevant facts and agreements among the parties in connection with the Arrangement. In issuing this opinion, we have relied on the facts and information Requestor presented to us and, in accordance with 42 C.F.R. § 1008.39(d), other publicly available information. This opinion is limited to the relevant facts Requestor presented to us, which we have not independently investigated, and the other publicly available information we reviewed in connection with our assessment of the Arrangement.

Based on the relevant facts certified in your request for an advisory opinion and supplemental submissions, as well as certain publicly available information, we conclude that: (i) although the Arrangement would generate prohibited remuneration under the Federal anti-kickback statute if the requisite intent were present, OIG will not impose administrative sanctions on Requestor in connection with the Arrangement under sections 1128A(a)(7) or 1128(b)(7) of the Act, as those

sections relate to the commission of acts described in the Federal anti-kickback statute; and (ii) the Arrangement does not generate prohibited remuneration under the Beneficiary Inducements CMP.

This opinion may not be relied on by any person[1] other than Requestor and is further qualified as set out in Part IV below and in 42 C.F.R. Part 1008.

I. FACTUAL BACKGROUND

A. The Product and Treatment Centers

Requestor is a pharmaceutical manufacturer that offers gene therapies for severe genetic diseases. Relevant to the Arrangement:

- The U.S. Food and Drug Administration ("FDA") has approved the use of the Product as a gene therapy for the treatment of [redacted] ("Condition A") in patients ages 12 and older. Condition A is the most severe form of [redacted]; patients with Condition A are dependent on regular blood transfusions to avoid severe anemia and, when the patient is a child, debilitating developmental complications. Requestor certified that the Product is a one-time, potentially curative treatment for Condition A.[2]

- The FDA has approved the use of the Product as a gene therapy for the treatment of [redacted] ("Condition B") in patients ages 12 years and older with recurrent vaso-occlusive crises ("VOCs"). Condition B is a genetic blood disorder that affects the shape of the patient's blood cells and can make blood cells stickier than usual. When blood cells stick to one another, they can form clusters in the bloodstream. These clusters block the flow of blood and oxygen, which can damage the blood vessels and organs. These blockages can lead to VOCs. Requestor certified that the Product is a one-time, potentially curative treatment for Condition B.[3]

There are multiple treatment stages for Condition A and Condition B patients who are treated with the Product:

- Initial Consultation and Care Management. The patient must undergo one or more consultations with a physician at an approved hospital treatment center ("Treatment Center") to determine eligibility for treatment with the Product. When a physician determines treatment with the Product is medically necessary, and the patient (or the patient's caregiver(s)) elects to move forward with such treatment, then a

[1] We use "person" herein to include persons, as referenced in the Federal anti-kickback statute and Beneficiary Inducements CMP, as well as individuals and entities, as referenced in the exclusion authority at section 1128(b)(7) of the Act.

[2] According to Requestor, in clinical trials for Condition A, the Product eliminated transfusion dependence for 91.4% of patients.

[3] [Redacted]

physician at the Treatment Center prescribes the Product for the patient and subsequently oversees the patient's entire treatment program. In addition to determining eligibility and overseeing treatment, the treating physician manages the patient's medical care throughout treatment and recovery, in consultation with a Treatment Center's care team. There will be a limited number of Treatment Centers that provide treatment with the Product; consequently, there also will be a limited number of physicians who can administer the Product.

- Blood Transfusions. The patient may undergo red blood cell transfusions, which happen prior to the next step of mobilization and apheresis (as described below).

- Mobilization and Apheresis. The patient's stem cells are mobilized and collected over the course of approximately 1 week at the Treatment Center. More than one round of mobilization and apheresis may be needed to collect enough cells to manufacture a sufficient dose of the Product.[4]

- Creation of the Product. The Product is made specifically for each patient, using the patient's own blood stem cells that are edited.

- Conditioning. Patients undergo chemotherapy-based fully-myeloablative conditioning ("Conditioning") prior to treatment with the Product, which clears existing blood stem cells from the bone marrow so they can be replaced with the edited cells. Conditioning can result in significant acute side effects, including, but not limited to, neutropenia, thrombocytopenia, leukopenia, anemia, and lymphopenia.

- Infusion/Hospital Stay. The Product's FDA-approved label ("Drug Label") indicates that patients are required to stay in the Treatment Center for 4 to 6 weeks (times may vary) after infusion with the Product. The Drug Label requires the patient to remain in the Treatment Center for this extended period of time so that the patient's health care team can closely monitor the patient's recovery.

The use of the Product carries a risk of serious potential complications including: (i) delayed platelet engraftment; (ii) neutrophil engraftment failure; and (iii) hypersensitivity reactions, including anaphylaxis. The Drug Label instructs health care providers to: (i) monitor absolute neutrophil counts and to manage infections since neutropenia places patients at high risk for infection; and (ii) monitor patients for hypersensitivity reactions during and after infusion. Alternative treatments to the Product are available for Condition A and Condition B patients and there is ongoing research that may expand the availability of alternative treatments for Condition A and Condition B patients.[5]

[4] Mobilization refers to the process by which hematopoietic stem cells are stimulated out of the bone marrow and into the bloodstream.

[5] [Redacted]

Requestor has begun to activate Treatment Centers; Requestor plans to activate 50 Treatment Centers in the first 18 months following Product approval and may add additional Treatment Centers in the future. Requestor selected Treatment Centers based on several objective criteria, including: (i) experience with Condition A and Condition B patients; (ii) location in areas with a high prevalence of Condition A and Condition B; (iii) experience with stem cell transplantation; (iv) capacity to treat patients on an inpatient basis; and (v) accreditation by the Foundation for the Accreditation of Cellular Therapy. Before a site is activated as a Treatment Center (i.e., when the site can begin treating patients with the Product), it must pass a quality audit conducted by Requestor.

There is a Treatment Center locator tool on Requestor's website to assist patients with identifying a Treatment Center. Using this tool, patients are able to input their city, state, and zip code (or some combination thereof) and receive a list of at least three Treatment Centers that are closest to them geographically. The Treatment Center locator lists the Treatment Centers in order of proximity to the patient and does not take into consideration the number of Condition A or Condition B patients that have received the Product at a Treatment Center or any other information with respect to the volume or value of patient referrals to or from a Treatment Center.

B. The Arrangement

Requestor offers the Arrangement to patients, including Federal health care program enrollees: (i) who are residents of the United States or a U.S. Territory; (ii) whose income is at or below 600 percent of the Federal Poverty Level; (iii) who meet program distance requirements, as described further below; (iv) who state that they do not have any assistance for travel, lodging, and associated expenses that may be covered by their insurer or be available through the Treatment Center or third-party charitable assistance; and (v) who have an on-label prescription for the Product. Requestor offers the Arrangement to patients during the: (i) mobilization and apheresis; (ii) Conditioning; and (iii) infusion/hospital stay phases of treatment with the Product. Requestor does not offer the Arrangement to patients during the initial consultation(s) or pre-mobilization red blood cell transfusions. The Arrangement, consisting of the following, is offered to one patient and one caregiver for patients ages 26 years and older, or to one patient and two caregivers for patients under 26 years of age:

- Airfare or Ground Transportation. Requestor covers round-trip airfare with coach/economy seating for patients and caregivers living 300 miles or more away from the nearest Treatment Center that is accepting new patients. In addition, Requestor will cover ground transportation costs for patients and caregivers living between 100 miles (or 2 hours driving distance) and 300 miles away from the nearest Treatment Center that is accepting new patients.

- Lodging. Requestor covers one room at a modest hotel for patients and caregivers living more than 100 miles or 2 hours driving distance from the nearest Treatment Center that is accepting new patients.

- Other Support During Treatment Center Stay. Requestor provides: (i) up to $50 per person, per day, to cover meals and authorized expenses during the patient's gene therapy

> treatment for patients and caregivers living more than 100 miles or 2 hours driving distance from the nearest Treatment Center that is accepting new patients; and (ii) up to $50 (in total, not per caregiver) for daily expenses related to parking, taxi or ride-sharing application rides, and gas associated with visiting the patient at the Treatment Center (i.e., while the patient is admitted to the Treatment Center). To receive this support for meals and authorized expenses, patients and caregivers are required to submit receipts to Requestor (either in writing or electronically), documenting authorized expenses actually incurred by the patient or caregiver(s).

Requestor certified that offering the Arrangement to caregiver(s)—which is intended to enable the caregiver(s) to remain near the Treatment Center during a patient's treatment with the Product—may positively impact the patient. According to Requestor, patients often suffer from complications associated with Condition A and Condition B, including anxiety and depression. Furthermore, citing to results from a recent study involving lay caregivers and patients who received stem cell transplants,[6] Requestor contends that patients with a dedicated caregiver have improved survival rates compared to patients without a caregiver.

The Arrangement is implemented and administered by Requestor and a travel vendor, which arranges for or books: (i) ground transportation (e.g., rental car or train) or air travel (as applicable); and (ii) lodging. Requestor reimburses patients and caregivers for meals and authorized expenses in the amounts authorized by Requestor following its expense verification process.

Requestor certified that it will not provide the Arrangement when insurance (e.g., Medicaid or Medicaid managed care)[7] or Treatment Center support is available.[8] In cases where partial support is available through the patient's insurance, including Medicaid, the Treatment Center,

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[6] Yaena Song et al., It Takes a Team to Make It Through: The Role of Social Support for Survival and Self-Care After Allogeneic Hematopoietic Stem Cell Transplant, FRONT PSYCHOL. (Mar. 2021).

[7] See 42 U.S.C. § 1396a(a)(4); 2021 Consolidated Appropriations Act, Pub. L. No. 116-260, § 209, 134 Stat. 2986 (2021); 42 C.F.R. § 431.53; 42 C.F.R. § 440.170.

[8] Requestor certified that it will not rely on a representation from the patient to identify whether a patient is eligible to receive support for travel, lodging, meals, and associated expenses from a third-party payor but instead will perform a benefits investigation to identify available assistance from third-party sources, including State Medicaid programs, to ensure the Arrangement does not provide support that is otherwise available from third-party sources. We express no opinion regarding Requestor's use of a benefits investigation to confirm that duplicate support is not provided to patients eligible for the Arrangement. In the event Requestor utilizes a benefits investigation to confirm that duplicate support is not provided to patients, such benefits investigation must comply with applicable Federal and State laws, including, without limitation, the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations.

or any other source, Requestor will limit the Arrangement to items not covered by such third-party sources.

Requestor does not advertise the Arrangement beyond providing Treatment Centers, potential referring physicians, and patients with a general overview of the patient support resources that are available for qualifying patients. Requestor certified that it will not use the Arrangement as a marketing tool to drive product selection, utilization, or referrals. Requestor further certified that it will not require either treating physicians or Treatment Centers to prescribe or use the Product exclusively.

II. LEGAL ANALYSIS

A. Law

1. Federal Anti-Kickback Statute

The Federal anti-kickback statute makes it a criminal offense to knowingly and willfully offer, pay, solicit, or receive any remuneration to induce, or in return for, the referral of an individual to a person for the furnishing of, or arranging for the furnishing of, any item or service reimbursable under a Federal health care program.[9] The statute's prohibition also extends to remuneration to induce, or in return for, the purchasing, leasing, or ordering of, or arranging for or recommending the purchasing, leasing, or ordering of, any good, facility, service, or item reimbursable by a Federal health care program.[10] For purposes of the Federal anti-kickback statute, "remuneration" includes the transfer of anything of value, directly or indirectly, overtly or covertly, in cash or in kind.

The statute has been interpreted to cover any arrangement where one purpose of the remuneration is to induce referrals for items or services reimbursable by a Federal health care program.[11] Violation of the statute constitutes a felony punishable by a maximum fine of $100,000, imprisonment up to 10 years, or both. Conviction also will lead to exclusion from Federal health care programs, including Medicare and Medicaid. When a person commits an act described in section 1128B(b) of the Act, OIG may initiate administrative proceedings to impose civil monetary penalties on such person under section 1128A(a)(7) of the Act. OIG also may initiate administrative proceedings to exclude such person from Federal health care programs under section 1128(b)(7) of the Act.

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[9] Section 1128B(b) of the Act.

[10] Id.

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

2. Beneficiary Inducements CMP

The Beneficiary Inducements CMP provides for the imposition of civil monetary penalties against any person who offers or transfers remuneration to a Medicare or State health care program beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier for the order or receipt of any item or service for which payment may be made, in whole or in part, by Medicare or a State health care program. OIG also may initiate administrative proceedings to exclude such person from Federal health care programs. Section 1128A(i)(6) of the Act defines "remuneration" for purposes of the Beneficiary Inducements CMP as including "transfers of items or services for free or for other than fair market value." Section 1128A(i)(6) of the Act contains an exception to the definition of "remuneration" that may apply in the context of the Arrangement. Section 1128A(i)(6)(F) of the Act provides that, for purposes of the Beneficiary Inducements CMP, the term "remuneration" does not include "remuneration which promotes access to care and poses a low risk of harm to patients and Federal health care programs (as defined in section 1128B(f) and designated by the Secretary under regulations)" (the "Promotes Access to Care Exception"). We have interpreted this provision to apply to:

> [i]tems or services that improve a beneficiary's ability to obtain items and services payable by Medicare or Medicaid, and pose a low risk of harm to Medicare and Medicaid beneficiaries and the Medicare and Medicaid programs by—(i) [b]eing unlikely to interfere with, or skew, clinical decision making; (ii) [b]eing unlikely to increase costs to Federal health care programs or beneficiaries through overutilization or inappropriate utilization; and (iii) [n]ot raising patient safety or quality-of-care concerns . . . .[12]

B. Analysis

1. Federal Anti-Kickback Statute

The Arrangement implicates the Federal anti-kickback statute in two ways. First, the assistance for certain travel, lodging, meals, and associated expenses constitutes remuneration to patients—including Federal health care program enrollees—that may induce them to purchase the Product. Second, by enabling patients—including Federal health care program enrollees—and their caregiver(s) to travel to, and stay near, a Treatment Center that the patient may not otherwise have selected for treatment, the Arrangement constitutes remuneration to the Treatment Centers and the treating physicians in the form of the opportunity to earn fees related to administering the Product, which may induce Treatment Centers to recommend, and physicians to order, the Product. No safe harbor applies to the streams of remuneration resulting from the Arrangement.

However, for the combination of the following reasons, we believe the risk of fraud and abuse presented by the Arrangement is sufficiently low under the Federal anti-kickback statute for OIG to issue a favorable advisory opinion.

[12] 42 C.F.R. § 1003.110 (defining "remuneration").

First, the Arrangement removes a barrier to accessing medically necessary care that is furnished by Treatment Centers. Because only a limited number of facilities are qualified to become Treatment Centers, some patients may live a significant distance from the closest Treatment Center. The Arrangement facilitates access to the Product for Federal health care program enrollees by subsidizing travel expenses the patients otherwise would not be able to afford, thereby allowing the patients to receive potentially curative treatment.

Second, the Arrangement facilitates compliance with the Drug Label instructions for the patient to remain at a Treatment Center for an extended period of time (i.e., 4 to 6 weeks). An extended hospital stay after treatment with the Product is necessary so that the patient's health care team can monitor for potential complications, including: (i) delayed platelet engraftment; (ii) neutrophil engraftment failure; and (iii) hypersensitivity reactions, including anaphylaxis. Moreover, while we acknowledge that certain elements of the Arrangement benefit the caregiver(s), it is possible that, without this support, certain caregivers may not be able to remain with the patients for an extended period of time, and Requestor provided information to support its assertion that caregiver support may have a positive impact on patient outcomes such that the remuneration given to caregiver(s) under the Arrangement could ultimately benefit the patient.

Third, the Product is a one-time, potentially curative treatment, such that the Arrangement differs from remuneration provided in connection with problematic seeding arrangements. The Arrangement is distinguishable from arrangements that provide free product or other remuneration in connection with an initial dose of a drug to induce patients to continue purchasing the drug when it would be payable by a Federal health care program. The Product is a one-time treatment that likely would not lead to additional referrals, mitigating the risk that the Arrangement would result in inappropriately increased costs to Federal health care programs in the future.

Finally, the Arrangement includes additional safeguards that mitigate the risk of fraud and abuse. For example, Requestor's certification that it will not authorize the Arrangement for any expenses for which insurance (including Medicaid) or Treatment Center or third-party charitable assistance is available contributes to our conclusion that the Arrangement poses a low risk of fraud and abuse under the Federal anti-kickback statute. Requestor also certified that it does not require either treating physicians or Treatment Centers to prescribe or use its Product exclusively. This certification reduces the risk of inappropriate steering or inappropriate utilization of the Product. Furthermore, Requestor certified that it will not use its offer of the Arrangement as a marketing tool to drive product selection, utilization, or referrals.

2. Beneficiary Inducements CMP

Under the Beneficiary Inducements CMP, we must analyze whether Requestor knows or should know that the financial support it provides for travel, lodging, meals, and associated expenses under the Arrangement is likely to influence a beneficiary's selection of a particular provider, practitioner, or supplier for the order or receipt of any item or service for which payment may be made, in whole or in part, by Medicare or a State health care program. The facts here implicate the Beneficiary Inducements CMP because Treatment Centers and physicians practicing at Treatment Centers are providers and suppliers that recipients of the Arrangement could be induced to select.

The Arrangement constitutes remuneration to eligible patients, including State health care program beneficiaries. This remuneration, consisting of assistance for certain travel, lodging, meals, and associated expenses, is likely to influence patients to select a Treatment Center and a physician practicing at a Treatment Center over other providers and suppliers that are outside the Arrangement. Requestor should know that patients likely would be influenced to select a Treatment Center and a physician practicing at a Treatment Center over other providers and suppliers that are outside the Arrangement because, as Requestor certified, the Arrangement enables the patient to travel to the Treatment Center to obtain the Product and enables the caregiver(s) to remain near the Treatment Center during a patient's treatment with the Product. For the foregoing reasons, unless an exception applies, the Arrangement would generate prohibited remuneration under the Beneficiary Inducements CMP.

We conclude that the Arrangement satisfies the Promotes Access to Care Exception to the Beneficiary Inducements CMP. To reach this conclusion, we first must examine whether the remuneration that is offered under the Arrangement improves a beneficiary's ability to obtain items and services payable by Medicare or Medicaid. As noted above, several factors necessary for the safe administration of the Product may create barriers to accessing treatment with the Product. First, there are a limited number of Treatment Centers, as only facilities that meet certain objective criteria may be qualified as Treatment Centers. Second, consistent with the Drug Label, an extended inpatient stay at the Treatment Center is required (i.e., 4 to 6 weeks) after infusion with the Product so that the patient's health care team can monitor for side effects. For these reasons, it is likely that the support Requestor provides for certain travel, lodging, meals, and associated expenses could remove or reduce potential financial and geographic barriers to receiving the Product, and thus could improve a beneficiary's ability to obtain items and services payable by Medicare or Medicaid (when the Product is payable by Medicare or Medicaid).

Next, we must examine whether the Arrangement poses a low risk of harm to Medicare and Medicaid beneficiaries and the Medicare and Medicaid programs. The Promotes Access to Care Exception to the Beneficiary Inducements CMP states that remuneration poses a low risk of harm if it: (i) is unlikely to interfere with, or skew, clinical decision-making; (ii) is unlikely to increase costs to Federal health care programs or beneficiaries through overutilization or inappropriate utilization; and (iii) does not raise patient safety or quality-of-care concerns. First, the risk that the Arrangement interferes with, or skews, clinical decision-making or raises patient safety or qualify-of-care concerns is sufficiently low. This is because the Arrangement is designed to increase patient safety by assuring adequate patient monitoring, consistent with the Drug Label, following administration of the Product so that the patient can timely access medical care in the event the patient experiences serious side effects from the Product. Second, the Arrangement is unlikely to increase costs to Federal health care programs or beneficiaries through overutilization or inappropriate utilization because the Product is a one-time, potentially curative treatment. Third, the Arrangement does not raise patient safety or quality-of-care concerns, as it is designed to increase patient safety by facilitating compliance with the safety protocols set forth on the Drug Label. Therefore, we conclude that the Arrangement poses a low risk of harm and thus satisfies the Promotes Access to Care Exception to the Beneficiary Inducements CMP. The Arrangement thus does not generate prohibited remuneration under the Beneficiary Inducements CMP.

III. CONCLUSION

Based on the relevant facts certified in your request for an advisory opinion and supplemental submissions, as well as certain publicly available information, we conclude that: (i) although the Arrangement would generate prohibited remuneration under the Federal anti-kickback statute if the requisite intent were present, OIG will not impose administrative sanctions on Requestor in connection with the Arrangement under sections 1128A(a)(7) or 1128(b)(7) of the Act, as those sections relate to the commission of acts described in the Federal anti-kickback statute; and (ii) the Arrangement does not generate prohibited remuneration under the Beneficiary Inducements CMP.

IV. LIMITATIONS

The limitations applicable to this opinion include the following:

- This advisory opinion is limited in scope to the Arrangement and has no applicability to any other arrangements that may have been disclosed or referenced in your request for an advisory opinion or supplemental submissions.

- This advisory opinion is issued only to Requestor. This advisory opinion has no application to, and cannot be relied upon by, any other person.

- This advisory opinion may not be introduced into evidence by a person other than Requestor to prove that the person did not violate the provisions of sections 1128, 1128A, or 1128B of the Act or any other law.

- This advisory opinion applies only to the statutory provisions specifically addressed in the analysis above. We express no opinion herein with respect to the application of any other Federal, State, or local statute, rule, regulation, ordinance, or other law that may be applicable to the Arrangement, including, without limitation, the physician self-referral law, section 1877 of the Act (or that provision's application to the Medicaid program at section 1903(s) of the Act).

- This advisory opinion will not bind or obligate any agency other than the U.S. Department of Health and Human Services.

- We express no opinion herein regarding the liability of any person under the False Claims Act or other legal authorities for any improper billing, claims submission, cost reporting, or related conduct.

This opinion is also subject to any additional limitations set forth at 42 C.F.R. Part 1008.

OIG will not proceed against Requestor with respect to any action that is part of the Arrangement taken in good-faith reliance upon this advisory opinion, as long as all of the material facts have been fully, completely, and accurately presented, and the Arrangement in practice comports with the information provided. OIG reserves the right to reconsider the questions and issues raised in this advisory opinion and, where the public interest requires, to rescind, modify, or terminate this

opinion. In the event that this advisory opinion is modified or terminated, OIG will not proceed against Requestor with respect to any action that is part of the Arrangement taken in good-faith reliance upon this advisory opinion, where all of the relevant facts were fully, completely, and accurately presented and where such action was promptly discontinued upon notification of the modification or termination of this advisory opinion. An advisory opinion may be rescinded only if the relevant and material facts have not been fully, completely, and accurately disclosed to OIG.

Sincerely,

/Susan A. Edwards/

Susan A. Edwards
Assistant Inspector General for Legal Affairs