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September 11, 2017

Seema Verma
Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
Room 445-G
Hubert H. Humphrey Building
200 Independence Ave., SW
Washington, DC 20201

BY ELECTRONIC DELIVERY

Re: Medicare Program; Revisions to Payment Policies Under the Physician Fee Schedule and Other Revisions to Part B for CY 2018; Medicare Shared Savings Program Requirements; and Medicare Diabetes Prevention Program Model (CMS-1676-P)

Dear Administrator Verma:

The Minnesota Society of Clinical Oncology (MSCO) appreciates this opportunity to comment on the proposed rule published by the Centers for Medicare & Medicaid Services (CMS) related to payment policies under the Physician Fee Schedule (PFS) and other revisions to Part B for Calendar Year (CY) 2018 (the "Proposed Rule").¹ MSCO represents the interests of the majority of oncologists treating cancer in Minnesota, and is a chapter member of the Association of Community Cancer Centers (ACCC) and an affiliate of the American Society of Clinical Oncology (ASCO).

In our comments below, we recommend that CMS:

- Finalize its proposal to add the professional Picture Archiving and Communication System (PACS) workstation as a direct practice expense (PE) input for additional digital diagnostic imaging services;

ASCO STATE/REGIONAL
**AFFILIATE
PROGRAM**



¹ 82 Fed. Reg. 33,950 (July 21, 2017)

- Finalize its proposed payment rates for radiation therapy planning services;
- Finalize its proposal to establish separate payment for superficial radiation treatment planning and management;
- Not implement its proposed reductions in payment for drug administration;
- Assign a separate Healthcare Common Procedure Coding System (HCPCS) code and payment rate to each biosimilar product;
- Finalize its proposal to add certain billing codes to the list of approved Medicare telehealth services with appropriate payment for those services;
- Finalize its proposal to make the requirement to consult appropriate use criteria (AUCs) for advanced diagnostic imaging services effective no earlier than January 1, 2019, and provide additional guidance on how ordering professionals should convey the required information to furnishing professionals;
- Finalize its proposal to modify the parameters of the Physician Quality Reporting System (PQRS), Value-Based Payment Modifier (VM), and Electronic Health Record (EHR) incentive for the CY 2018 payment year;
- Not finalize its proposal to reduce payment for services provided in off-campus provider-based departments at 25 percent of the OPPS rates; and
- Proceed cautiously regarding any proposals drastically impacting future reimbursement.

I. CMS should finalize its proposal to add the professional PACS workstation as a direct PE input for additional digital diagnostic imaging services.

In the CY 2017 rulemaking, CMS added a professional PACS workstation as a direct PE input for certain digital diagnostic imaging services, based on a list of Current Procedural Terminology (CPT®²) codes that used the technical PACS workstation as a direct input, but excluding add-on codes, codes for non-diagnostic services, and image guidance codes where the dominant provider is not a radiologist. In the CY 2018 Proposed Rule, CMS proposes to add 26 CPT codes to the list of codes with the professional PACS workstation as a direct input, consisting of vascular ultrasound services that previously were excluded because a radiologist was not the dominant specialty provider.³ MSCO supports this proposal because it appropriately recognizes the use of the professional PACS workstation in these procedures now that physicians

² CPT is a registered trademark of the American Medical Association (AMA).

³ 82 Fed. Reg. at 33,959.

who perform them have largely transitioned from film to digital technology. We encourage CMS to finalize it.

II. CMS should finalize its proposed payment rates for radiation therapy planning services (CPT codes 77261, 77262, and 77263).

CMS proposes revised payment rates for radiation therapy planning services, identified as potentially misvalued through a screen of high-expenditure services across specialties.⁴ CMS proposes revised work relative value units (RVUs) based on the American Medical Association (AMA) RVU Update Committee (RUC) recommendations. CMS notes that it also considered much lower work RVUs for this family of codes based on a crosswalk between CPT code 77263 and CPT code 96111 (developmental testing, including assessment of motor, language, social, adaptive, and/or cognitive functioning by standardized developmental instruments), however. CPT code 96111 is entirely unrelated to radiation therapy, but CMS noted that the code had “identical intraservice time” and “similar total time” to the RUC-recommended time values for CPT code 77263, and therefore calculated alternative RVUs for the radiation therapy planning codes based on the crosswalk. CMS seeks comment on whether this alternative valuation would be more appropriate than the RUC-recommended RVUs.

MSCO strongly supports the RUC-recommended work RVUs and urges CMS to finalize its proposal. The RUC-recommended RVUs are based on consideration of the physician work required to provide *these* services, not unrelated services that may take a similar amount of time to complete. It would be inconsistent with the ordinary and appropriate procedure for valuing and reimbursing physician services under Part B to use an unrelated code as a crosswalk while disregarding the RUC’s recommendation on the appropriate work RVUs for the actual codes at issue. In addition, MSKO is deeply concerned that further cuts in payment to radiation oncology providers will make it difficult for some radiation oncologists, particularly those operating in rural and underserved areas, to maintain a full range of services or even to remain open at all. We urge CMS to finalize the RUC-recommended RVUs to ensure that payment remains adequate to maintain access to radiation oncology services for all Medicare beneficiaries.

III. CMS should finalize its proposal to establish separate payment for superficial radiation treatment planning and management (HCPCS code GRRR1).

CMS notes that it had previously solicited comment on a change in language for HCPCS code GRRR1 for superficial radiation treatment planning and management that meant that more services were being bundled with the code that had been billed separately. The RUC had not evaluated whether these modifications should change the valuation for these services. Due to an edit that no longer is active, evaluation and management (E/M) services billed with this code also commonly are denied payment by the Medicare Administrative Contractors (MACs).⁵

⁴ *Id.* at 34,002.

⁵ *Id.* at 34,012.

Because of these issues, CMS is proposing separate payment for professional treatment planning and management tied to this code and to add physician work and work time tied to radiation management services. CMS proposes to adopt the RUC-recommended inputs for this code with some adjustments and to make some modifications to the supply items associated with this code. MSCO appreciates CMS's thoughtful approach and encourages the agency to finalize its proposal.

IV. CMS should not implement its proposed reductions in payment for drug administration.

MSCO is deeply concerned about the proposed reductions in payment for many drug administration codes. Following review as potentially misvalued codes, CMS proposes to reduce payment for code 96402 (chemotherapy administration, subcutaneous or intramuscular; hormonal anti-neoplastic) by almost 12 percent. Payment for codes 96372 (therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular), 96374 (therapeutic, prophylactic or diagnostic injection IV push, single or initial substance/drug), and 96375 (therapeutic, prophylactic or diagnostic injection; each additional sequential IV push of a new substance/drug) would be reduced by 18 to 19 percent from 2017 to 2018 and could face further reductions in the future as CMS phases-in reductions in RVUs of 20 percent or more over a two-year period, as required by the statute.⁶ These reductions could harm access to care, especially in rural settings, and we urge CMS not to implement them. If the agency proceeds to implement them as proposed, we believe it is essential to monitor patient access to care.

MSCO supports CMS's proposal to activate code 96377 (application of on-body injector (includes cannula insertion) for timed subcutaneous injection) for payment under the PFS. This change in status for this code will help physicians be reimbursed for using this technology to treat beneficiaries with cancer.

V. CMS should assign a separate HCPCS code and payment rate to each biosimilar product.

In the CY 2016 PFS rulemaking, CMS finalized a payment methodology such that all biosimilars with the same reference product are assigned to a single HCPCS code and reimbursed based on the volume-weighted Average Sales Price (ASP) for all products under the code, plus six percent of the reference product's ASP.⁷ In the Proposed Rule, CMS does not propose to change its policy on payment for biosimilar products under the PFS, but requests comment on whether CMS's current policy is "fostering a robust and competitive marketplace and encouraging the innovation that is necessary to bring these products to the marketplace."⁸ CMS adds that it is interested in "better understanding if and how the innate differences in

⁶ SSA § 1848(c)(7); 82 Fed. Reg. at 33957.

⁷ 80 Fed. Reg. 70,886, 71,101 (Nov. 16, 2015).

⁸ 82 Fed. Reg. at 34,090-91.

biological products and their current regulatory environment should be reflected in Medicare payment policy for biosimilars, particularly as it relates to biosimilars that are licensed for fewer than all indications for which the reference product is licensed or situations where different biosimilars may be licensed for different subsets of indications for which the reference product is licensed.”⁹

MSCO appreciates CMS’s willingness to reconsider its policy on payment for biosimilar products. As we have stated in our previous comments on this issue, we believe that CMS should establish a policy that assigns a separate HCPCS code and separate payment rate to each biosimilar product. CMS’s current policy imposes unfair administrative burdens on providers who have to take extra time to ensure they are administering the correct product from among different biological products grouped under the same HCPCS code. The current policy also compromises access and quality of care by imposing undue financial pressures on providers to choose the least costly biological product rather than the one that is most clinically appropriate, because all biological products in the same HCPCS code are reimbursed at the same rate. CMS’s current policy also makes it more difficult for the Food and Drug Administration (FDA) to track safety information back to the manufacturer of the specific biosimilar product for which information is reported.

These unintended consequences of CMS’s current payment policy stifle the market for biosimilars by creating potential barriers to uptake among providers. They also show that the current policy fails to recognize the “innate differences in biological products,” as the Proposed Rule aptly puts it. Biosimilars are similar – but not identical – to other biological products with a common reference product, and CMS payment policy should recognize this fundamental aspect of biosimilars by establishing a separate code and separate payment for each product. This approach will ensure effective monitoring of the safety of each biosimilar product following approval and will encourage providers to focus on providing the best and most appropriate beneficiary care. We encourage CMS to propose and finalize such a policy at the earliest opportunity.

VI. CMS should finalize its proposal to add certain billing codes to the list of approved Medicare telehealth services, with appropriate payment for those services, and should work with MSKO and other stakeholders to establish broader coverage for telehealth services under the PFS.

CMS proposes to add three new services to the list of CPT codes eligible for Medicare payment when provided via telehealth, including HCPCS code G0296 (Counseling visit to discuss need for lung cancer screening using low dose CT scan (service is for eligibility determination and shared decision making)).¹⁰ CMS also proposes to add four CPT codes as add-on services to services that are already included on the telehealth list:

- CPT 90785 (interactive complexity (list separately in addition to the code for primary procedure));

⁹ *Id.* at 34,091.

¹⁰ *Id.* at 33,971-72.

- CPT 96160 (administration of patient-focused health risk assessment instrument with scoring and documentation, per standardized instrument);
- CPT 96161 (administration of caregiver-focused health risk assessment instrument for the benefit of the patient, with scoring and documentation, per standardized instrument)); and
- HCPCS G0506 (comprehensive assessment of and care planning for patients requiring chronic care management services (list separately in addition to primary monthly care management service)).

The Proposed Rule also solicits comment on whether the agency should make separate payment for CPT codes that describe remote patient monitoring (e.g., CPT 99091 (collection and interpretation of physiologic data digitally stored and/or transmitted by patient and/or caregiver to the physician or other qualified health care professional, qualified by education, training, licensure/regulation (when applicable) requiring a minimum of 30 minutes of time), and CPT codes that describe extensive use of communications technology (e.g., CPT 99090 (analysis of clinical data stored in computers (e.g., ECGs, blood pressures, hematologic data))).

MSCO strongly supports these proposals and encourages CMS to finalize them. CT lung cancer screening is a cost-effective diagnostic test proven to significantly reduce lung cancer deaths, and we believe that access to the related counseling visit via telehealth will improve patient access to it. In addition, as we have stated in the past, we believe that broader Medicare coverage for physician services provided via telehealth and remote patient monitoring is essential to ensuring access to care for Medicare beneficiaries in rural areas, allowing patients to receive care from specialists and sub-specialists who might otherwise be located too far away from the patient to participate in their care on a regular basis, and helping to meet increased demand for cancer care in our aging population. We urge CMS to work with MSCO and other provider organizations to educate physicians about expanded Medicare coverage for telehealth and remote monitoring. We also ask CMS to prioritize its consideration of any applications to add oncology-related services to the telehealth list.

VII. CMS should finalize its proposal to make the requirement to consult AUCs for advanced diagnostic imaging services effective January 1, 2019, and should provide additional guidance on how ordering professionals should convey the required information to furnishing professionals.

MSCO appreciates CMS's new proposals to continue implementation of the requirement to establish AUCs for certain advanced diagnostic imaging services (ADIS).¹¹ As health care providers who rely on such imaging services to diagnose and treat cancer patients, MSCO and its members look forward to working closely with CMS to implement the new AUC requirements in a manner that is practical, achievable, and consistent with the statute.

We appreciate CMS's proposal to make the requirement to consult AUC effective beginning January 1, 2019. Although some of our members already have implemented AUC

¹¹ *Id.* at 34,093-96.

programs for ADIS, most have not. They will need to invest significant time and resources to comply with the AUC requirements and contract with the developers of qualified clinical decision support mechanisms (CDSMs). CMS's proposal to delay the effective date until January 1, 2019, and then to allow an educational and operations testing period of one year during which CMS will continue to pay claims whether or not they correctly include the required information, should allow sufficient time for our members to comply with the requirements and intent of the program. We ask CMS to finalize these proposals accordingly.

To implement the reporting requirement, CMS proposes to establish a series of HCPCS level 3 G-codes. These G-codes would describe the specific CDSM that the ordering professional consulted. In addition, CMS would develop a series of modifiers to provide necessary information as to whether the imaging service adheres to the applicable AUC, does not adhere to such criteria, or such criteria were not applicable to the imaging service ordered, as well as whether a qualified CDSM was not used to consult AUC because an exception applies.¹² CMS does not explain how this information will be conveyed from the ordering professional to the furnishing professional, however, and we ask the agency to provide additional guidance on this issue in the final rule.

CMS's current regulations require that "[c]ertification or documentation . . . be generated each time an ordering professional consults a qualified CDSM" and "[i]nclude a unique consultation identifier generated by the CDSM."¹³ They also require all CDSM's to "[g]enerate and provide a certification or documentation at the time of order that documents which qualified CDSM was consulted; the name and national provider identifier (NPI) of the ordering professional that consulted the CDSM; whether the service ordered would adhere to specified applicable AUC; whether the service ordered would not adhere to specified applicable AUC; or whether the specified applicable AUC consulted was not applicable to the service ordered."¹⁴ MSCO asks CMS to consider whether including the unique consultation identifier on the ADIS order and later on the ADIS claim could replace the need for the G-codes and for the modifiers other than those necessary when an exception applies. We believe this could significantly reduce the administrative burden on both ordering and furnishing professionals.

Finally, we support CMS's proposal to automatically exempt from the AUC requirement ordering professionals who are exempt from the advancing care information category under the Quality Payment Program (QPP). This automatic exemption appropriately recognizes that such physicians either do not have control over the availability of the necessary EHR technology at their facility, do not have face-to-face patient interactions, or both. We support the continued availability of exemption through one or more of the other hardship factors as well. MSCO requests that CMS finalize these proposals.

VIII. CMS should finalize its proposal to modify the parameters of the PQRS, VM, and EHR incentive for the CY 2018 payment year.

¹² *Id.* at 34,094.

¹³ 42 C.F.R. 414.94(g)(1)(vi).

¹⁴ *Id.*

CMS proposes to modify the parameters of the PQRS, VM, and EHR incentive programs in the CY 2018 payment year to align those programs with the first year of the QPP, which replaced all three programs beginning with the CY 2017 performance year. With respect to the PQRS and EHR incentive, CMS proposes to reduce the minimum quality reporting requirement from nine measures to six measures and to eliminate the requirement that the reported measures cover three National Quality Strategy domains.¹⁵ With respect to the VM, CMS proposes to reduce the automatic negative adjustment for professionals who fail to meet minimum quality reporting requirements from -4.0% to -2.0% (for groups of 10 or more clinicians) and from -2.0% to -1.0% (for groups of 2 to 9 clinicians and solo practitioners). CMS also proposes to hold harmless from any negative adjustment all clinician groups and solo practitioners who met minimum quality reporting requirements, and to limit the maximum positive adjustment to two times the adjustment factor.¹⁶

MSCO supports these proposals. We support the ongoing effort to promote the delivery of higher-quality, cost-efficient care through the QPP and the legacy programs, and our members are actively engaged in CMS-sponsored models such as the Oncology Care Model (OCM) that hold the promise of reshaping health care to better serve patients and the Medicare program. As clinicians enter the first few years of the QPP and invest significant time and resources in adjusting to the new program's requirements, we believe it is appropriate for CMS to make these changes to the final year of the legacy programs, and we urge CMS to finalize them.

IX. CMS should not finalize its proposal to reduce payment for services provided in off-campus provider-based departments at 25 percent of the OPPS rates.

MSCO strongly opposes CMS's proposal to establish payment for nonexcepted off-campus hospital departments at 25 percent of the OPPS rates. The proposed rate does not accurately reflect the cost of care in these departments, and it is inconsistent with Congressional intent for these sites to be reimbursed under a system other than the OPPS to create parity with physicians' offices. If implemented, these payment reductions would harm access to care and severely limit hospitals' ability to extend services at locations that would be more convenient for beneficiaries.

Sections 1833(t)(1)(B)(v) and (t)(21) of the Social Security Act (SSA) established that certain items and services furnished by certain "nonexcepted" off-campus outpatient departments must be paid for under a system outside of the OPPS.¹⁷ For CY 2017, CMS determined that the applicable payment system is the PFS, but due to differences in the services offered by these departments and physicians' offices and claims processing issues, CMS established new rates under the PFS at 50 percent of the OPPS rate.¹⁸ CMS established this "relativity adjuster" after performing an evaluation of the most frequently billed services at provider-based departments

¹⁵ 82 Fed. Reg. at 34,099; 34,104.

¹⁶ *Id.* at 34,125.

¹⁷ SSA §§ 1833(t)(1)(B)(v) and (t)(21)

¹⁸ 81 Fed. Reg. 79,562, 79,723, 79,725 (Nov. 14, 2016).

and comparing payment for those services under the PFS and OPFS.¹⁹ CMS determined that overall the PFS payment rate for the 25 most frequently billed services at provider-based departments ranged between 0 percent and 137.8 percent of the OPFS, with a volume weighted average of 45 percent.²⁰ CMS recognized that this analysis was based on imperfect data, but decided to proceed anyway with a payment rate for these departments of 50 percent of the OPFS.²¹

CMS proposes to reduce the relativity adjuster to 25 percent for CY 2018. If implemented, these rates would be far less than the PFS rates for many services that are essential to cancer care. For example, CPT code 96413 (chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug) would be reimbursed at \$143.60 in a physician office but only \$71.65 in a non-excepted off-campus department, including payment for drugs that are not separately payable under the OPFS. Payment for CPT code 74177 (Computed tomography, abdomen and pelvis; with contrast material(s)), including payment for the contrast agent that is packaged under the OPFS, would be only \$84.79 in a non-excepted department, compared to payment of \$221.34 for the technical component in a physician's office, plus separate payment for the contrast agent.

MSCO urges CMS to not implement the proposed 25 percent relativity adjuster because it would produce payments that are not representative of the payments that would be made under the PFS and would not fairly reflect the cost of care in these departments. In proposing to now adopt a payment rate of 25 percent of the OPFS, CMS does not cite any new data or perform any additional analyses. In fact, CMS acknowledges that it is not able to study the CY 2017 claims data that might allow the agency to consider numerous factors that affect the comparison between PFS and OPFS rates, including OPFS packaging policies.²² Instead, CMS bases its proposal on the evaluation of the OPFS payment rate for a single service—HCPCS code G0463, for certain clinic visits—instead of a more comprehensive review of payment at provider-based departments.²³ CMS uses this evaluation as the sole basis for its proposal despite recognizing in the CY 2017 final rule that “these payment rates are not entirely comparable” because of the “more extensive packaging that occurs under the OPFS for services provided along with clinic visits” compared to the PFS.²⁴ CMS provides no explanation for its apparent conclusion that a payment adjustment based on only these two codes is appropriate now when it was not appropriate last year. CMS notes only that it is concerned that the current 50 percent relativity adjuster might overestimate payments.

Even if CMS is not yet prepared to perform a full analysis of what the payment rate for services at provider-based departments should be, it cannot arbitrarily reduce the payment rate for these departments by half compared to the rate in CY 2017 without justifying its reasons for

¹⁹ *Id.*

²⁰ *Id.* at 79,724.

²¹ *Id.* at 79,725.

²² 82 Fed. Reg. at 33,983.

²³ *Id.* at 33,982–83.

²⁴ 81 Fed. Reg. at 79,723.

doing so. The agency has presented no grounds for concluding that a payment rate of 50 percent of the OPPS is too high and therefore should not adopt the payment reduction for provider-based departments as final.

In addition, the proposed rates are entirely inconsistent with Congressional intent. Contrary to Congress's intent to establish parity between reimbursement for services provided in these departments and services provided in physicians' offices, this proposal would create large differences in payment between these settings of care. For example, drugs and biologicals currently paid for separately under the PFS often are packaged for purposes of the OPPS. When payment for these drugs is packaged into a drastically reduced payment for a drug administration, these drugs and biologicals would be reimbursed at a fraction of the payment available for them under the PFS, amounting to grossly inadequate reimbursement to hospitals for drugs and biologicals provided through these departments. This cannot be the intent of Congress in establishing an alternative payment system for off-campus outpatient departments.

MSCO therefore urges CMS to not finalize the proposed payment reduction and to reconsider its relativity adjuster in general. We further note that we would be happy to work with CMS to develop the data necessary to ensure that provider-based departments are adequately reimbursed.

X. CMS should proceed cautiously regarding any proposals drastically impacting future reimbursement because it takes physicians years of planning to accommodate these changes and adjust to changes in technology and payment systems

In the Proposed Rule, CMS requests information on the agency's "flexibilities and efficiencies" as a step toward starting a "national conversation about improvements that can be made to the health care delivery system that reduce unnecessary burdens for clinicians, other providers, and patients and their families."²⁵ CMS explains that it aims "to increase quality of care, lower costs, improve program integrity, and make the health care system more effective, simple and accessible."²⁶ MSCO thanks CMS for this opportunity to provide our recommendations on how to achieve these important goals.

Cancer diagnosis and treatment are continuously evolving, and we are at a time of particularly important advancements in the technologies available to treat cancer. Increasingly personalized medicine and new gene therapies have the potential to exceed the efficacy of prior therapies, and oncology practices and hospitals need to continue to adapt to changing diagnostic and treatment protocols to use these tools most effectively. At the same time, our members are working to improve treatment using existing drugs, through expanded patient education and counseling, better coordination among specialists, participation in clinical trials, and prolonged office hours.

²⁵ 82 Fed. Reg. at 34,172.

²⁶ *Id.*

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We also are experiencing significant changes in the systems used to pay for cancer care. CMS and other payers continue to move away from traditional fee-for-service models to value-based approaches. In addition to adjusting to the Quality Payment Program, oncology practices participating in the Oncology Care Model (OCM) have dedicated considerable resources to making this model successful. Each participant in the OCM must analyze its patient population, the services it offers, and anticipated reimbursement and costs to identify ways to provide high quality care more efficiently over several years.

Many of our members have made investments in technology and staffing based on expected future reimbursement levels, but frequent changes in the conventional Medicare payment systems, including the PFS and the OPSS, that form the basis for the OCM and other new payment models, create challenges for participants in these models. For example, large reductions in payment for the drug administration and hydration services that are central to many cancer treatment regimens, whether through revaluation under the PFS, proposed expansions of packaging in the OPSS, or reductions in payment to nonexcepted off-campus departments, can upend a practice or hospital's plans to expand services over the coming years and complicate efforts to achieve the improvements in care that are the heart of the OCM and other new payment models.

It is difficult to plot a path forward toward new payment and care delivery models when CMS keeps changing the terrain. MSCO and its members want to continue to work with CMS to improve the quality and efficiency of care provided to Medicare beneficiaries. We embrace the opportunity to adopt new treatment options and develop new payment models, but we also recognize that stability and predictability in the payment systems that serve as the foundations for these models is essential to achieving these goals. We ask CMS to use its regulatory flexibilities to provide stable reimbursement throughout the transition to new payment models. For example, CMS should consider exempting participants in the OCM or other value-based models from proposed payment reductions, such as the reduction in payment for nonexcepted off-campus departments. CMS also should phase-in significant reductions in RVUs under the PFS over several years, reducing the maximum reduction in a single year from 19 percent to no more than 10 percent.

* * *

Thank you for this opportunity to share the oncology provider perspective on your proposals in the PFS Proposed Rule. Please feel free to contact Leah Ralph at (301) 984-5071 if you have any questions or need any additional information. Thank you again for your attention to this very important matter.

Respectfully submitted,



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President, MSCO