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LIVING TECHNOLOGY

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September 6, 2013

VIA Electronic Submission to http://www.regulations.gov

Marilyn Tavenner,
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS-1601-P
Mail Stop C4-26-05
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: CMS-1601-P: Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Hospital Value- Based Purchasing Program; Organ Procurement Organizations; Quality Improvement Organizations; Electronic Health Records (EHR) Incentive Program; Provider Reimbursement Determinations and Appeals

Section II.A.3.c(2): Drugs and Biologicals That Function as Supplies or Devices When Used in a Surgical Procedure

Dear Ms. Tavenner:

Organogenesis is pleased to submit comments on the Outpatient Prospective Payment System (OPPS) proposed rule for calendar year 2014.[1] Organogenesis is a leading regenerative medicine company and the developer and manufacturer of Apligraf, a living, bi-layered, cellular technology.

In this rule, CMS proposes a new policy to package certain drugs and biologicals that it characterizes as functioning as supplies or devices when used in a surgical procedure. The only items affected by this proposal are products that CMS identifies as "skin substitutes", a group that encompasses both basic dressing and covering products used in wound management and a smaller group of advanced therapeutic products, including Apligraf, that are used to treat wounds.

[1] "Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Hospital Value-Based Purchasing Program; Organ Procurement Organizations; Quality Improvement Organizations; Electronic Health Records (EHR) Incentive Program; Provider Reimbursement Determinations and Appeals", 78 Fed. Reg. 43534 – 43707, July 19, 2013.

We strongly disagree with this proposal for the following reasons:

1. Apligraf is a Specified Covered Outpatient Drug (SCOD) and CMS lacks the legal authority to package SCODs or arbitrarily classify them as supplies;
2. Products like Apligraf that are used to treat wounds are the "primary therapeutic modalities" and are not surgical supplies used in a primary procedure and CMS' proposal is inconsistent with other packaging policies that exclude therapeutic products from packaging;
3. Apligraf is not used as an implant and is not similar to currently packaged implantable biologics;
4. The proposed OPPS payment rate for skin substitute procedures does not adequately reflect the cost of wound treatment products such as Apligraf and would not pay hospitals for Apligraf at its acquisition cost, thereby hindering access to this important therapeutic modality;
5. The proposal will jeopardize patient access to important therapeutic options, increase Medicare spending, and stifle future innovations in wound care; and
6. The proposed policy would limit Medicare's ability to implement coverage determinations.

Therefore, we strongly recommend that CMS not finalize the policy as proposed. If CMS moves forward with packaging skin substitute products, the agency should revise its policy to package only those products that are dressings or coverings with Food and Drug Administration (FDA) clearance for the management of wounds (510K devices or Human Cell and Tissue Products [HCT/P]). **CMS should exclude products such as Apligraf that meet the following conditions:**

- **Are SCODs; and**
- **Are approved by the FDA as wound treatments (through Premarket Approval [PMA],Biologic License Application[BLA], or New Drug Application [NDA]).**

For these products, CMS should retain its current payment methodology of ASP + 6 percent. We describe our reasons and recommendations in greater detail below.

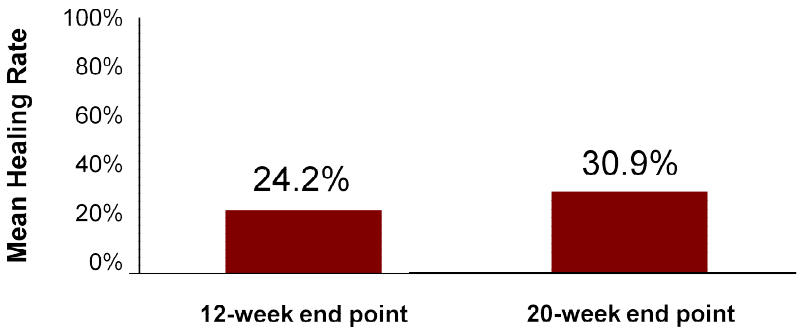
Treatment of Chronic Ulcers

Ulcers of the lower extremities that fail to heal, or heal extremely slowly, are a serious and widespread health problem. They are the most common chronic wounds, with an estimated prevalence between 1 and 1.3 percent of the world population and 2.5 million people in the United States. Often leading to osteomyelitis and amputation, they are a major cause of disability in people with diabetes, and the annual cost to the healthcare system to treat such wounds runs to billions of dollars. The availability of safe and effective treatments for these wounds is therefore of significant public health concern.

For example, even with optimal standard wound care, healing neuropathic ulcers in patients with diabetes continues to be a challenge. As Figure 1 shows below, at twelve weeks, the chances of healing neuropathic diabetic foot ulcers (DFUs) with conventional therapy, including use of basic dressings, is only 24 percent. At 20 weeks, the healing rate is only 31 percent.[2]

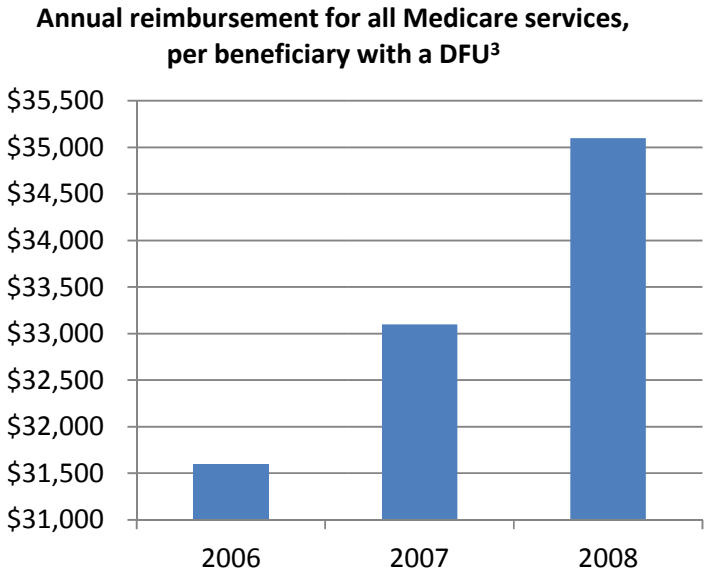
[2] Margolis DJ, et al. *Diabetes Care*. 1999;22(5):692-695.

Figure 1
Low DFU Healing Rates with Conventional Therapy



Those who develop DFUs can be affected by debilitating complications and incur higher healthcare costs. Complicated DFUs, particularly those that lead to lower leg amputations, increase Medicare cost significantly and those costs have been rising over time (Figure 2). In 2008, Medicare is estimated to have spent more than $35,000 per beneficiary with a DFU. [3]

Figure 2



To provide high quality care and help avoid the trauma and added cost of amputations, clinicians need to have access to the full range of options for healing DFUs. It is important to remember that, except for

[3] Agency for Healthcare Research and Quality; 2011. Publication 10(11)-EHC009-2-EF.

Apligraf and Dermagraft, the products identified by CMS as skin substitutes are used to treat a wide variety of skin ulcers and are wound dressings and coverings that are part of standard care. As discussed more fully below, Apligraf and Dermagraft are not interchangeable with such products. Instead Apligraf and Dermagraft are used to treat wounds that have failed to heal after receiving standard care, often as a therapy of last resort.

Background on Apligraf and Other Products

We disagree with any classification of skin substitute products that includes Apligraf and Dermagraft in the same class as wound management products. Apligraf a living, bi-layered, cellular technology that was originally approved by the FDA in 1998 as a Class III pre-market approval (PMA) therapeutic product. The approved indications for use include the following:

- Apligraf is indicated for use with standard therapeutic compression for the treatment of non-infected partial and full-thickness skin ulcers due to venous insufficiency of greater than 1 month duration and which have not adequately responded to conventional ulcer therapy; and
- Apligraf is indicated for use with standard diabetic foot ulcer care for the treatment of full-thickness neuropathic diabetic foot ulcers of greater than three weeks duration which have not adequately responded to conventional ulcer therapy and which extend through the dermis but without tendon, muscle, capsule, or bone exposure.

We note that Apligraf's approved indications are for "treatment" of certain wounds which have not responded to conventional therapy, including wound dressings. One other product, Dermagraft, is a living, uni-layer cellular technology that is also approved under a PMA for the treatment of diabetic foot ulcers that have not responded to conventional therapy. The FDA approval of both Apligraf and Dermagraft is supported by evidence from large, multi-center clinical trials.

This evidence base and approval as a therapeutic product sets Apligraf and Dermagraft apart from the numerous other products broadly identified as "skin substitutes". Other products are biosynthetics or acellular, animal-derived products that are cleared by FDA under 510(k) authority or are human, donor tissue products that are regulated as human cells, tissues, and cellular and tissue-based products (HCT/P) under Section 361 of the Public Health Service Act. The intended use of the 510(k) products is in the management, not the treatment, of wounds. These products are sometimes referred to as "wound coverings" or "dressings", terms which are not appropriately applied to Apligraf and Dermagraft. Wound dressings and coverings are part of standard care – they aid healing by fostering a moist wound environment and providing a barrier against contamination, giving the wound a chance to heal of its own accord. By contrast, Apligraf is living tissue that interacts with a wound and releases growth factors – cytokines and other biologically active products that stimulate healing and cause the wound to heal faster and more completely. Apligraf is indicated for use after standard care efforts have proved unsuccessful at healing the wound. Apligraf is not clinically interchangeable with wound dressings or coverings.

The table below shows the classification of products done by the Agency for Healthcare Research and Quality (AHRQ).

Table 1
AHRQ Classification of "Skin Substitutes"[4]

Origin/ Composition	Products	FDA Regulation	Intended Use
Living human and/or animal tissues and cells	Apligraf®, Dermagraft®	PMA	"Treatment" of specific chronic wounds (i.e., non-infected, >1 month in duration, and unresponsive to conventional treatment)
Acellular animal-derived	Acell, Aongen™, Atlas, Avagen, Collagen Sponge, Collagen Wound Dressing, Collaguard®, CollaSorb™, CollaWound™, Collexa®, Collieva®, Coreleader, Dermadapt ™, DressSkin, E-Z Derm, EndoForm, Excellagen, FortaDerm™, HA Absorbent Wound Dressing, Helicoll, Integra, LTM Wound Dressing, MatriStem, Matrix, Medline Collagen, Oasis®, Primatrix™, SIS Wound Dressing II, SS Matrix™, Stimulen, TheraForm, Unite®	510(k)	"Management" of wounds
Biosynthetic	Hyalomatrix®, Jaloskin®, Suprathel®, Talymed®	510(k)	"Management" of wounds
Human donor tissue, minimally processed	AlloDerm, AlloPatch HD™, Alloskin™, Cymetra®, Dermacell®, Arthroflex®, Flex HD®, GammaGraft®, Graftjacket®, Matrix HD, Memoderm™, Puros®, Repliform ®, TheraSkin®	361 HCT/P	n/a

An important distinction between these categories is that 510k or HCT/P products have not generated and submitted the clinical evidence required to obtain an FDA approval for treating wounds. Products cleared via the 510(k) process are reviewed by FDA only for their equivalence to other legally marketed products (in this case, wound *coverings*), while Section 361 HCT/Ps undergo no premarket scrutiny for

[4] AHRQ Technology Assessment, "Skin Substitutes for Treating Chronic Wounds, December 2012.

safety or efficacy at all. None of these products, therefore, has been reviewed by FDA for its efficacy in actively healing wounds. FDA has made clear that many of the Section 361 HCT/Ps that have been marketed for wound treatment are not being legally marketed and those products would require premarket approval to be able to be promoted for such claims.[5]

CMS Lacks the Legislative Authority to Package Apligraf

CMS proposes to package certain drugs and biologicals that it characterizes as functioning as "supplies or devices in a surgical procedure."[6] Apligraf is a specified covered outpatient drug (SCOD) as defined in section 1833(t)(14)(B) of the Social Security Act, because it was paid as a pass-through biological on or before December 31, 2002. The law requires that in 2006 and subsequent years, SCODs be paid based on "the average acquisition cost for the drug for that year." [7] [emphasis added] Most other products CMS identifies as skin substitute do not meet the definition of SCODs because they became eligible for pass-through payments beginning January 1, 2003 or later. We are attaching an analysis of the Secretary's authority to package Apligraf to this comment letter and incorporate its contents by reference so it is part of the administrative record (see Attachment 1). The analysis concludes that CMS lacks the authority to package Apligraf and Dermagraft because they are SCODs. Under the law, CMS must pay SCODs on the basis of its own average cost, not on the average cost of non-SCODs.

CMS also does not have the authority to change the classification of a product from "SCOD" to "supply". The term "supply" is not defined in statute but was defined by CMS in the preamble to the interim final rule establishing the OPPS as "Surgical dressings used during surgery, or other treatments in the hospital outpatient setting that are also paid under the DMEPOS fee schedule."[8] Apligraf is not a supply under this definition. Apligraf is not a surgical dressing and is not paid under the DMEPOS fee schedule. CMS affirmatively determined Apligraf is not a supply by granting the product pass-through status, which is not available to supplies.

In sum, as a threshold matter, CMS does not have the legal authority to package Apligraf and Dermagraft because they are SCODs and because CMS cannot arbitrarily reclassify Apligraf and Dermagraft as supplies due to its long standing policy of treating those products as drugs.

CMS Does Not Recognize the Therapeutic Nature of Apligraf

As noted, Apligraf is approved by the FDA as a therapeutic product for the treatment of certain non-healing wounds. Apligraf is affixed to chronic wound via a procedure termed an "application". Apligraf is not ancillary to or supportive of the "application" procedure – it is the reason the procedure is being

[5] For example, FDA advised Surgical Biologics, a MiMedx Group Company, that its injectable human amniotic membrane allograft products (marketed under the trade names AmnioFix™ Injectable, AccelShield™ Injectable, and EpiFix™ Injectable, which have been marketed for, among other things, reducing inflammation and scar tissue formation, and enhancing wound healing of soft tissues, requires FDA premarket approval before it may be legally marketed. (Letter from Mary A. Malarkey, Director of the Office of Compliance and Biologics Quality in FDA's Center for Biologics Evaluation and Research, to Bill Taylor, President and CEO, Surgical Biologics, a MiMedx Group Company (August 28, 2013).)

[6] 78 FR 43571 – 72

[7] §1833(t)(14)(A)(iii)(I)

[8] 65 Fed Reg 18444 (April 7, 2000).

performed. In this way it is a "primary therapeutic modality", similar to therapeutic radiopharmaceuticals, which are exempted from packaging.

In the proposed rule, CMS inverts the relationship between the procedure and the treatment, making the product ancillary to the service required to furnish it. CMS states: "Because a skin substitute must be used to perform any of the procedures described by a CPT code in the range 15271 through 15278, … skin substitute products serve as a necessary supply for these surgical repair procedures."[9] By this logic, all non-self-administered drugs are supplies for the procedures used to administer them. For example, chemotherapy drugs would be supplies for the injection or infusion code with which they are reported.

Apligraf Is Not an Implant

We agree with CMS that some of the wound management products are used as supplies incident to a surgical procedure and are, or are analogous to, biological implants currently packaged under the OPPS. Some of those products are marketed for both surgical implant applications (e.g. tendon repair) and dressings for wound management. For example, MatriStem products can be used for wound management and as surgical matrices. Such products may be similar to implantable biologics that are already packaged under the OPPS. However that is not true of Apligraf, which is a therapeutic treatment for cutaneous wounds and is not approved or ever used for surgical implant applications. We agree with CMS that products that are marketed for and used as both biological implants in invasive surgical procedures such as tendon repair as well as for the management of wounds should be packaged. However, products such as Apligraf, which are never used in an invasive surgical procedure, are only used to treat DFUs and venous stasis ulcers, and have nothing in common with implantable biologics, should not be packaged.

Proposal Inappropriately Assumes Interchangeability of Products and Will Jeopardize Patient Care

In its proposal, CMS does not recognize that Apligraf and Dermagraft are not clinically interchangeable with any of the other products that CMS terms skin substitutes. The premise of the proposed approach assumes that the different products can be used interchangeably: "[W]here there are a variety of devices, drugs, items, supplies, etc. that could be used to furnish a service, some of which are more expensive than others, packaging encourages hospitals to use the most cost-efficient item that meets the patient's needs, rather than to routinely use a more expensive item, which often results if separate payment is provided for the items."[10] This statement fails to recognize that the more expensive products are not, in fact, interchangeable with the less expensive products. The higher cost of Apligraf and Dermagraft reflects differences in the indicated use of the products and the quality and quantity of evidence supporting those uses.

The variation in cost between the wound management skin substitute products and the wound treatment products such as Apligraf and Dermagraft is significant. The table below shows the 2012 claims data for the three most commonly used products: Apligraf, Dermagraft, and Oasis, the most frequently used wound management product (Table 2). Together these products account for 86 percent of the roughly 87,600 claims for products identified as skin substitutes.

[9] 78 FR 43572
[10] 78 FR 43568 – 69

Table 2
Utilization, Cost, and Payment Data for Three Most Frequently Used Products[11]

Product	2012 OPPS Claims	2013 ASP+6	Per Day Cost (Drug)	Per Day Cost (Drug + Procedure(s))	2014 Proposed Payment	Difference
Apligraf	28,777	$39.58	$1,904	$2,242	$862	($1,380)
Dermagraft	22,625	$42.55	$1,652	$1,990	$862	($1,128)
Oasis	24,229	$8.21	$137	$388	$862	$474

Costs are not distributed evenly across these products but are instead grouped into two extremes: Oasis has a per day cost that is less than a tenth of the cost of Apligraf and Dermagraft. When there is a bimodal distribution of costs as are seen across the products in Table 2, packaging is not an appropriate policy. Packaging Apligraf and Dermagraft with the less expensive wound coverings and dressings will ensure that Medicare pays incorrectly for every application procedure it covers. The proposed 2014 payment rates will overpay for every use of Oasis by $474 and will underpay every use of Dermagraft by $1,128 and every use of Apligraf by $1,380. The financial losses will be exacerbated when treating large wounds, creating an incentive not to treat the sickest patients with proven advanced therapeutics.

We have attached an analysis of the Medicare claims data that illustrates the dramatic differences in total cost for procedure code 15271 *Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or les wound surface area* when only other skin substitute products are included in the packaging and when Apligraf and Dermagraft are also included (see Attachment 2).[12] The total procedure costs with Apligraf and Dermagraft are almost twice the procedure costs if only other skin substitutes are included and the packaged cost of the skin substitute products is more than four times greater with Apligraf and Dermagraft than when Apligraf and Dermagraft are excluded. This is additional evidence that the cost of these products is a bimodal

[11] CMS OPPS Cost Statistics Files, July 1, 2013 Addendum B update, and 2014 NPRM Addendum B.
[12] Memo from Mary Jo Braid-Forbes to Antonio Montecalvo (September 6, 2013). We note that this analysis uses arithmetic rather than geometric mean costs but the relationship between the costs are expected to be the same using both measures.

distribution which means that Medicare will consistently overpay or underpay depending on which of the products is used.

Under the current payment policy that provides for separate payment for most skin substitute products, hospitals have no incentive to make decisions about product use other than based on clinical need. The packaging proposal would change that dynamic and create a strong financial disincentive that would deter hospitals/clinics from using evidence-based therapeutic products, even with patients for whom conventional treatment has been unsuccessful. Conversely, there will be strong financial incentives to overuse inexpensive, basic dressings or coverings that lack substantial clinical evidence.

The result of this proposal will likely be an increase in Medicare spending for two reasons. First, in the short term, as noted, hospitals will be significantly overpaid for every use of packaged wound management products. Such overpayment will occur for patients that would have been likely to receive those products under the ASP+6 percent payment methodology and will also incentivize use of those products with other patients, leading to an increase in both the cost per patient as well as the volume of services compared to the current methodology. In addition, by dramatically underpaying for Apligraf and Dermagraft, the proposal will severely restrict access to those products for patients who have already failed conventional treatment. Without access to appropriate treatment options to help heal DFUs or ulcers caused by venous insufficiency, such patients will be more likely to develop complications and require costly ongoing care, again adding to Medicare's total spending.

The Proposal Will Undermine Innovation

Developing effective treatments for chronic wounds has been a longstanding unmet medical need in the US. Organogenesis pioneered the field of advanced wound care. Apligraf was the first advanced wound treatment approved by the FDA for patients with diabetic foot ulcers and venous stasis ulcers whose ulcers failed to heal with standard care. The development of Apligraf took over 10 years and costs tens of millions of dollars. Organogenesis has spent millions of dollars on research for new uses of Apligraf and to develop other advanced wound care products. The CMS packaging proposal will make it impossible for Organogenesis and other companies to develop new advanced wound care products or to discover new uses for existing products. Specifically the packaging proposal will make it impossible for Organogenesis to afford ongoing research. Without revenue from appropriate reimbursement, Organogenesis and other manufacturers will not explore advances in wound treatment and care for this hard-to-treat population will stagnate rather than progress.

Proposal Will Restrict CMS' Ability to Implement Coverage Determinations

CMS does not propose to require that hospitals include a Q code for a skin substitute product when providing a skin substitute procedure. Instead, elsewhere in this rule, CMS proposes to eliminate requirements that hospitals include packaged device or radiopharmaceutical procedure codes when reporting certain procedures. Such requirements ensure that the costs of those items are appropriately reflected in the claims data. Hospitals may continue to report the packaged codes but will have little incentive to do so.

We expect that, if CMS packages skin substitute products as proposed, instead of reporting specific Q codes, hospitals will most likely report costs under a "surgical supply" or other cost center. Without the

Q codes, CMS and its contractors will not be able to determine what product was used. Local coverage determinations by various Medicare contractors do not cover specific products that lack clinical evidence to support medical necessity. The packaging proposal will make it difficult, if not impossible, for contractors to enforce their coverage determinations. Under the bundling proposal, CMS will be without the ability to identify specific products and Medicare will most likely pay for items that conflict with its published coverage determinations.

Recommendation

Because of the significant concerns described above, we strongly recommend that CMS not finalize the policy as proposed. If CMS moves forward with packaging skin substitute products, the agency should revise its policy to package only those products that are dressings or coverings with Food and Drug Administration (FDA) clearance for the management of wounds (510K devices or Human Cell and Tissue Products [HCT/P]). **CMS should exclude products such as Apligraf that meet the following conditions:**

- **Are SCODs; and**
- **Are approved by the FDA as wound treatments (through Premarket Approval [PMA],Biologic License Application[BLA], or New Drug Application [NDA]).**

For these products, CMS should retain its current payment methodology of ASP + 6 percent. We describe our reasons and recommendations in greater detail below.

We understand that at the August meeting of the Advisory Panel on Hospital Outpatient Payment, the Panel recommended that CMS postpone adoption of the packaging provisions from the proposed rule, including packaging of drugs and biologicals that function as supplies or devices in surgical procedures. Given the wide scope of CMS' proposals and the myriad of concerns with the skin substitute proposal alone, we concur with this recommendation and urge CMS to accept it. However, we note that therapeutic wound care products should not be included in any packaging proposals that may be considered in future rulemaking.

We appreciate the opportunity to comment on this important issue.

Sincerely,

Gary S. Gillheeney, Sr.
Executive Vice President, Chief Operating Officer,
and Chief Financial Officer

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Date:	September 5, 2013
To:	Barbara Fisher, Deputy Associate General Counsel Office of the General Counsel Department of Health & Human Services
From:	Thomas R. Barker Brian P. Carey
Regarding:	Payment of Apligraf® As a Specified Covered Outpatient Drug Under the Statutory Default in the Hospital Outpatient Prospective Payment System

I. Overview

Our client Organogenesis Inc. has asked us to prepare this legal memorandum, which provides our analysis of the statutory authority of the Centers for Medicare & Medicaid Services (CMS) to package the payment of the skin substitute Apligraf® – a biological product meeting the statutory definition of a Specified Covered Outpatient Drug – as proposed in the CY 2014 Hospital Outpatient Prospective Payment System (HOPPS) Proposed Rule.[1] Organogenesis is the manufacturer of Apligraf®, a biological product used to heal skin ulcers, such as diabetic foot and venous leg ulcers, that are not healing after three to four weeks, despite treatment with conventional wound therapies.

It is our conclusion that, based on the clear and unambiguous language of the Social Security Act, CMS does not have the legal authority to package Apligraf® with an associated outpatient surgery in which the product is used, nor can Apligraf® be treated identically to, and placed in the same APC with, other biological or cell tissue based products used in an outpatient surgery. A central premise of both Medicare payment policy and administrative law is that CMS may not change a payment method for a drug or biological where that method is established by statute, even when CMS believes that it has a policy reason for that change.

[1] 78 Fed. Reg. 43,534, 43,571 (July 19, 2013).

Here, Congress has already established a statutory payment scheme for a specific category of drugs and biologicals, which includes Apligraf®. These "*specified covered outpatient drugs*" (SCODs) must be paid separately based upon a precise statutory scheme. In point of fact, Apligraf® has been paid separately under this scheme since the methodology became effective in 2006. Furthermore, the agency has adopted a "statutory default" under section 1833(t)(14)(A)(iii)(II) of the Social Security Act which authorizes payments to be equal to the payment rates established under the methodology described in sections 1842(o), 1847A, or 1847B of the Act (generally, average sales price, or ASP) when the average acquisition cost of a SCOD is not available. Indeed, in the very Proposed Rule to which this memorandum is directed, CMS confirmed this precise policy: SCODs are to be paid based on the statutory default under Section 1847A at ASP plus 6%.[2] Thus, CMS is required to pay Apligraf® — a single source biologic — at ASP plus 6%, and only sales of Apligraf® may be used to calculate the ASP payment.

This legal memorandum will be submitted as a formal comment to CMS in support of the detailed clinical and policy grounds that Organogenesis will submit in a separate comment letter in opposition to the proposed packaging policy for Apligraf®. Based on these collective arguments, we request that the agency not package Apligraf® in the Final Rule, and pay Apligraf® separately based on the Average Sales Price (ASP) methodology as required by statute.

II. Clinical Overview of Apligraf® and Background on Medicare Payment History

A. Clinical Overview of Apligraf®

Apligraf® is a unique, bioengineered, cell-based biological for the treatment of chronic, hard-to-heal venous leg ulcers and diabetic foot ulcers. Like human skin, it is made from living cells and it is composed of two layers, a dermis and an epidermis, comprised of healthy, functioning, responsive cells that stimulate the wound to heal. Apligraf® is the only active wound-healing product approved by the U.S. Food and Drug Administration (FDA) to treat both venous leg ulcers and diabetic ulcers.[3] On May 22 1998, the FDA approved Apligraf® for marketing under its pre-market approval (PMA) process for "use with standard therapeutic compression for the treatment of non-infected partial and full-thickness skin ulcers due to venous insufficiency of greater than adequately responded to conventional ulcer therapy."[4] Multiple supplements have been added since the first approval, including an indication for treating diabetic foot ulcers.

Pursuant to FDA's regulations, Organogenesis conducted significant and extensive clinical testing in order to demonstrate that Apligraf® is safe and effective for healing

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[2] Id. at 43,607-09.

[3] Other skin substitutes, most of which are not SCODs, are also paid separately under HOPPS, based on a longstanding CMS policy. Id. at 43,608.

[4] FDA CDRH, *Summary of Safety and Effectiveness Data: Apligrapf*, *available at* http://www.accessdata.fda.gov/cdrh_docs/pdf/P950032b.pdf.

diabetic foot ulcers that are present for at least three weeks and venous leg ulcers that are present for at least one month. The Apligraf® diabetic foot ulcer pivotal study included more than 200 patients with diabetic foot ulcers of at least two to three weeks duration. This pivotal study found clear evidence that nearly 50% of patients treated with Apligraf® experienced complete wound closure during the first eight weeks of treatment. In addition, the incidence of complete wound closure was higher for patients receiving Apligraf® during the first eight weeks as opposed to those patients in the control group that were treated with conventional measures. Similarly, the Apligraf® venous leg ulcer pivotal study included over 200 patients at multiple centers throughout the country with ulcers present at least one month. This pivotal study demonstrated significant wound closure during the first eight weeks of treatment and a greater incidence of complete wound closure for patients treated with Apligraf® as opposed to patients in the control group. The FDA reviewed this clinical data and approved Apligraf® specifically for the treatment of venous leg ulcers of greater than one month duration and diabetic foot ulcers of greater than three weeks duration.

B. Medicare Payment History of Apligraf® as a Biological

The Medicare payment history of Apligraf® demonstrates that Apligraf® has been recognized and paid as a biologic for more than 13 years and as a SCOD since the 2004 implementation of the Medicare Modernization Act of 2003. This background may help clarify for the agency the classification of Apligraf® in the hospital outpatient setting as a separately payable SCOD. In 2001 and 2002 Apligraf® was paid in the hospital outpatient setting as a biological under the pass through list.[5] In February, 2001 CMS (then HCFA) issued a Program Memorandum (Transmittal B-01-07) that states "Apligraf® has met the statutory requirement as a biologic."[6] (See attachment 1). Following the enactment of the Medicare Prescription Drug, Improvement and Modernization Act of 2003 Apligraf® has been paid in the hospital outpatient setting as a sole source biological at 88% of AWP in 2004 and 83% of AWP in 2005 under the specified covered outpatient drug provision.[7] Apligraf® was included in the Government Accountability Office (GAO) survey in 2005 of acquisition costs for hospital outpatient drugs as a specified covered outpatient drug. [8] Since

[5] 65 Fed. Reg. 67,798, 67,837 (November 13, 2000). (See attachment 2).

[6] Apligraf® meets the statutory definition of a biological. Under Section 1861(t)(1), the term "biological product" includes such biologicals "as are included (or approved for inclusion) in the United States Pharmacopoeia" and other compendia, or are approved by the pharmacy and drug therapeutics committee of the Medical staff of the hospital furnishing the biological for use in the hospital. Apligraf® was approved for inclusion in the United States Pharmacopoeia in 2000, and is therefore a biological.

[7] 69 Fed. Reg. 819, 823 (January 6, 2004). The interim finale rule implementing the Medicare Modernization Act of 2003 lists Apligraf® as a "Sole Source Drug" in Table 1. The rule states in relevant part "The sole source category is defined in section 1833(t)(14)(F)(i) of the Act as a biological product (as defined under section 1861(t)(1) of the Act) or a single source drug (as defined in section 1927(k)(7)(A)(iv)) of the Act)." (See attachment 3.)

[8] (GAO-05-581R) Medicare Hospital Outpatient Drug Prices, June 30, 2005. The GAO Report on specified covered outpatient drugs states "[GAO] obtained from our survey data the average and median purchase prices for each of the 53 SCOD drug categories." Apligraf® is listed under number 38 in Table 1 of the GAO report detailing the categories of SCODs. (See attachment 4.)

2006 Apligraf® has been payable as a SCOD biological under the ASP methodology. Since 2013 Apligraf® has been paid under the statutory default provisions of 1833(t)(14)(A)(iii)(II) of the Act at ASP plus 6%.

When Apligraf® is administered to a Medicare beneficiary incident to a physician's services, the payment methodology under Section 1847A is the ASP methodology. Thus, Apligraf® has consistently been separately payable as a biological in the Part B setting since 2005.

III. HOPPS Procedural Background

On July 19, 2013, CMS published in the Federal Register the Hospital Outpatient Prospective Payment System (HOPPS) Proposed Rule for calendar year 2014.[9] In the Proposed Rule, CMS announced its intention to begin packaging certain skin substitutes with their associated surgeries, on the basis that "skin substitutes . . . function as supplies or devices that are used in surgical procedures and, therefore, should be packaged with the surgical procedure in which the products are used."[10] The agency proposes to revise its regulations at 42 C.F.R. § 419.2(b)(4) to include skin substitutes as an example of a packaged surgical supply. The proposed rule acknowledges that currently skin substitutes are separately paid in the OPPS as biologicals, pursuant to the ASP methodology, and are subject to the drug and biological packaging threshold. In the Proposed Rule, CMS compresses more than fifty different products with varying indications and modalities into a single, broad category of "skin substitutes." The text of the Proposed Rule does not refer to Apligraf®. However, Apligraf® is listed in Addendum P for those codes to be packaged under this proposal and assigned to status indicator "N" for CY 2014.

In the rule CMS proposes that "skin substitute products [] be unconditionally" packaged. However, the proposed rule does acknowledge that these skin substitute products would continue to be paid under the statutory requirements for "pass-through status" for new skin substitutes that meet the pass-through criteria. As discussed in more detail below in Section V., the proposed rule fails to acknowledge that certain skin substitutes, including Apligraf®, meet the statutory definition of a SCOD and must continue to be paid under that statutory scheme.

As explained below, Apligraf®'s unique status as a SCOD and therapeutic make it inappropriate for packaging as both a statutory and policy matter.

[9] *Supra*, n. 1.

[10] Id. at 43,572.

IV. The Statute and CMS Precedent Prohibit Packaging Apligraf®

A. The Social Security Act Requires a Unique Payment Methodology for SCODs like Apligraf®

Congress has "minutely detailed the reimbursement rates" for most drugs and biologicals.[11] In the case of SCODs, section 1833(t)(14)(A)(iii) of the Social Security Act specifies one such reimbursement rate. Under that statute, CMS is required to pay separately drugs and biologicals that meet the statutory definition of a SCOD under a specific statutory payment scheme. As set out below in detail, under the agency's own determination and practice, Apligraf® meets this statutory definition and has been separately payable as a SCOD since 2004. Therefore, absent a change in the statute, CMS is precluded from altering this "minutely detailed" payment methodology for Apligraf® by means of regulation.

Section 1833(t)(14)(B) of the Social Security Act defines a SCOD as a drug or biological (or radiopharmaceutical) used in hospital outpatient departments, and for which CMS has established a separate ambulatory payment classification (APC) group. In addition to these criteria, the statute narrows the scope of a SCOD to include only those drugs or biologicals paid for on a pass-through basis on or before December 31, 2002. CMS has recognized Apligraf® as a SCOD since 2004.[12] Apligraf® was first separately payable under APC 1305 in 2000.[13] Additionally. Apligraf® received its first pass-through payment on January 1, 2001, prior to the statutory deadline. Importantly, as discussed in detail in Section V., most other skin substitutes are not SCODs, as they did not begin receiving pass-through payments until after January 1, 2003.[14]

The CMS proposal to package payment for Apligraf® with other products based on hospital claims is exactly the opposite of what Congress sought to establish with the SCOD special payment status. Congress revised the hospital outpatient payment for certain drugs and biologics as part of the MMA, due to concerns over payment for these drugs and biologicals under the HOPPS APCs based on claims data.[15] To remedy concerns about hospital underpayment, Congress established a clear statutory formula that was intended to capture the average acquisition costs associated with each individual qualifying product. The Act thus establishes that in all years subsequent to 2005, the payment rate for SCODs "shall

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[11] Hays v. Sebelius, 589 F.3d 1279, 1286 (D.C. Cir. 2009) (quoting Hays v. Leavitt, 583 F. Supp. 62, 71 (D.D.C. 2008)).

[12] 69 Fed. Reg. 819, 823 (January 6, 2004).

[13] 65 Fed. Reg. 67,798, 67,837 (November 13, 2000).

[14] Based on our review, the only other skin substitute that meets the definition of a SCOD is Dermagraft®. See 65 Fed. Reg. 67,798, 67,837 (November 13, 2000) (setting payment rate for Apligraf®® at $1,157.81). See also 66 Fed. Reg. 59,856, 60,051 (November 30, 2001) (setting payment rate for Dermagraft® at $577.60).

[15] Pub. L. No. 108-173 § 621, 117 Stat. 2066, 2307- 11 (Dec. 8, 2003). The House Ways and Means Committee report on the earlier version of the bill explains that the new payment methodology for SCODs was being enacted in response to a lack of uniformity in reimbursing outpatient drugs. According to the report, the problem was that "[h]ospital charges were not designed to specifically capture the resource costs for specific items." H.R. Rep. No. 108-178 at 227.

be equal . . . to the average acquisition cost for the drug for that year . . . as determined by the Secretary taking into account the hospital acquisition cost survey data under subparagraph (D)" (emphasis supplied). Section 1833(t)(14)(A)(iii). Under subparagraph (D), the Act also specifically requires that the Secretary's cost survey must "generate a statistically significant estimate of the average hospital acquisition cost for each specified covered outpatient drug" (emphasis supplied). Since its CY 2006 HOPPS Final Rule, CMS has set average acquisition cost based on data reported under the ASP methodology pursuant to section 1847A.[16]

The statute is thus clear and unambiguous: where a drug or biological qualifies as a SCOD, its payment "shall" be based on the average acquisition cost for the drug — not based on the average acquisition cost of the larger APC to which the drug is assigned and not based on the cost of other drugs. Thus, CMS cannot package together multiple skin substitutes with Apligraf®, as doing so would not reflect the average acquisition cost of Apligraf® — as required by statute — but would instead reflect the average cost of whatever items are used with the associated procedure. Moreover, the Act emphasizes Congress's drug-specific focus again in subparagraph (D), expressly requiring that the Secretary's cost survey determine the average hospital acquisition cost for each SCOD. Had Congress intended the Secretary's survey to determine average acquisition cost for each APC, Congress could easily have done so.[17] Instead, Congress emphasized, in two different places in the statute, that the cost and reimbursement calculations for SCODs must be drug-specific.[18]

B. CMS's "Statutory Default" Methodology Sets Apligraf® Payment at ASP Plus 6%.

The statutory payment for Apligraf® is a two step analysis. As we have shown above, the first step is that Apligraf® meets the statutory definition of a SCOD. The second step is which statutory payment methodology for a SCOD the agency elects to assign. Initially, the agency determined payment for SCODs based on a determination of "the average acquisition cost of the drug for that year."[19]

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[16] 77 Fed. Reg. 68,210, 68,389 (Nov. 15, 2012).

[17] Indeed, the legislative history of (MMA) lends further support to the Congressional intent that SCODs be reimbursed separately. According to the Conference Report, "[i]t is the intent of the conference that products eligible payment under the hospital outpatient department section include all products paid by Medicare on a pass-through list as a drug or biologic prior to December 31, 2002." 149 CONG. REC. 22, 30,373 (2003). The current CMS proposal to package SCODs would achieve the exact opposite result, by favoring certain drugs over others, even where some drugs are more appropriate for certain patients.

[18] It is a fundamental tenet of statutory construction that Congress knows how to say what it means. See, e.g., Meghrig v. KFC Western, Inc., 516 U.S. 479, 485 (1996) ("Congress . . . demonstrated in CERCLA that it knew how to provide for the recovery of cleanup costs, and . . . the language used to define the remedies under RCRA does not provide that remedy"); National Bank v. New York, 347 U.S. 373, 378 (1954) (finding "no indication that Congress intended to make this phase of national banking subject to local restrictions, as it has done by express language in several other instances").

[19] *See* 70 Fed. Reg. at 68,516, 68,642 (Nov. 10, 2005) (describing choice to use average acquisition cost methodology).

In the 2013 Final HOPPS rule, CMS made a significant determination to alter the statutory payment methodology of SCODs. While the impact of the payment rate was only minimal, the determination by the agency is significant for the calculation of the Apligraf® payment amount. In that final rule, the agency implemented for the first time the statutory requirements of section 1833(t)(14)(A)(iii)(II) of the Act to require an alternative methodology for determining payment rates for SCODs. This provision states that if hospital acquisition cost data are not available, payment shall be equal (subject to any adjustment for overhead costs) to payment rates established under the methodology described in section 1842(o), section 1847A, or section 1847B of the Act. As previously explained, pursuant to sections 1842(o) and 1847A of the Act, Part B drugs are paid at ASP plus 6 % when furnished in physicians' offices.

In that 2013 final rule, CMS established the "statutory default" methodology for determining payment rates for SCODs.[20] Under this "statutory default" CMS reverted to the alternative methodology under section 1833(t)(14)(A)(iii)(II), which authorizes payments to be equal to the payment rates established under the methodology described in sections1842(o), 1847A, or 1847B. CMS concluded that this "statutory default" resulted in a payment rate of ASP+6 for SCODs in CY 2013.[21] In the CY 2014 Proposed Rule, CMS again proposes to apply this statutory default payment methodology of ASP plus6 % to "all separately payable drugs and biologicals, which include SCODs."[22]

The adoption of the statutory default under HOPPS further supports the conclusion that Apligraf® cannot be packaged and must be paid based on its own ASP. CMS explained the rationale for implementing the statutory default language was that "we believe that establishing the payment rates based on the statutory default of ASP plus 6% is appropriate as it yields increased predictability in payment for separately payable drugs and biologicals under the OPPS."[23] Moreover, the agency stated the policy was also necessary in order to harmonize payment for drugs and biologics in the hospital outpatient and physician office setting.[24] In the physician office setting, under section 1847A(c)(6)(D), to qualify as a "single source drug or biological," a product must either be a "biological" or a "drug which is not a multiple source drug and which is produced and distributed under a new drug application." As previously mentioned, Apligraf® meets the statutory definition under the Social Security Act of a biological, having been approved for inclusion in the United States Pharmacopeia in 2000.[25] Because Apligraf® is a biological, it meets the statutory definition of a single source drug.

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[20] 77 Fed. Reg. 68, 210, 68,386 (Nov. 15, 2012).

[21] Id.

[22] 78 Fed. Reg. 43,534, 43,608 (July 19, 2013).

[23] Id..

[24] 77 Fed. Reg. 68,210, 68,386 (November 15, 2012).

[25] *See supra* n. 8. Under section 1861(t)(1) of the Act, the term "biological product" includes such biologicals "as are include (or approved for inclusion) in the United States Pharmacopeia" and other compendia, or are

Under section 1847A(b)(4) — one of the statutory provisions covered by the "statutory default" — payment for single source drugs must be based on the lesser of ASP or wholesale acquisition cost for that drug. In contrast, for multiple source drugs, ASP is determined on the basis of the volume-weighted average of the sales of all drugs "including within the same multiple source drug billing and payment code."[26] Apligraf® has been consistently paid under the ASP methodology based on its own reported sales data since CY 2006. Because of the statutory default in section 1833(t)(14)(A)(iii)(II), under which CMS has properly paid for Apligraf® in prior years, CMS must continue to pay Apligraf® at ASP plus 6%.

C. SCODs Are Different Than Other Drugs and Biologicals

The statutory definition for SCOD expressly limits the scope of its application to a narrowly defined class of products. In addition to establishing the three statutory requirements discussed above, Congress explicitly excluded a wide range of products. In particular, the statute states "Such term does not include— a drug or biological for which payment is first made on or after January 1, 2003, under paragraph (6)."[27] Therefore, the vast majority of outpatient drugs and biologicals paid under the HOPPS system since 2003 do not, and will not, qualify for special payment status as a SCOD. Apligraf®, however, is not among those vast majority of outpatient drugs and biologicals.

CMS explicitly acknowledges this difference in rulemakings over the years, and refers to it again in the Proposed Rule. As a matter of policy, the agency has decided to treat all separately payable drugs and biologicals as SCODs, but it is only required to do so for products that meet the statutory language. On this point the agency notes in the Proposed Rule "it has been our longstanding policy to apply the same treatment to all separately payable drugs and biologicals, which include SCODs, and drugs and biologicals that are not SCODs."[28] The agency reinforces this point by further stating that "although we do not distinguish SCODs in this discussion, we note that we are required to apply section 1833(t)(14)(A)(iii)(II) of the Act to SCODs, but we also are applying this provision to other separately payable drugs and biologicals, consistent with our history of using the same payment methodology for all separately payable drugs and biological."[29]

Therefore, although CMS may exercise policy discretion to propose to expand the special payment status of SCODs to a broader class of drugs and biologicals, it may not do what it has done here: narrow the class of SCODs from those drugs or biologicals which meet the statutory definition of that term.

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approved by the pharmacy and drug therapeutics committee of the Medical staff of the hospital furnishing the biological for use in the hospital."

[26] Social Security Act § 1847A(b)(3).

[27] *Id*. at § 1833(t)(14)(B)(ii)(I).

[28] 78 Fed. Reg. 43,534, 43,609 (July 19, 2013).

[29] Id.

* * *

In sum, the proposal to package Apligraf® would be contrary to both the statutory plain language and to Congressional intent. Apligraf® is a SCOD pursuant to the Act, and under CMS' Proposed Rule must be reimbursed based on the "statutory default" methodology of ASP plus6%. Absent legislative changes to section 1833(t)(14), CMS simply lacks the statutory authority to implement the approach proposed in the Proposed Rule.

V. Apligraf® Cannot Be Packaged Because it Does Not Function as a "Supply" and is Therapeutically Different from Other Skin Substitutes

A. Apligraf® Does not Function As A Supply

As noted above, the fundamental flaw in the proposal for packaging of skin substitutes is the failure to address the requirements of payment as a SCOD for certain products including Apligraf®. The Proposed Rule only makes a general statement that "Currently skin substitutes are separately paid in the OPPS as if they are biologicals according to the ASP methodology." CMS goes on in the Proposed Rule, and purports to rely on its general authority to package medical devices, medical and surgical supplies, and surgical dressings into the related procedure under 42 C.F.R. § 419.2(b)(4) in order to package all skin substitutes.[30] To the extent that one of those skin substitutes is Apligraf®, CMS may not adopt its proposal.

Quite simply, Apligraf® also does not meet the definition of medical and surgical supplies, as it functions instead as a therapeutic. Moreover, Apligraf® has different clinical indications and characteristics that differ from the other skin substitutes. We discuss both points below.

Neither the HOPPS statute nor the regulation contain any explicit definition of a "supply," but in the original HOPPS rulemaking in 2000, CMS described "supplies" as "surgical dressings used during surgery or other treatments in the hospital outpatient setting that are also paid under the DMEPOS fee schedule."[31] Apligraf® is neither a surgical dressing nor has it ever been paid under the DMEPOS fee schedule. Rather, Apligraf® is a therapeutic modality, indicated for the treatment of non-infected partial and full-thickness skin ulcers. Unlike other SCODs that have been packaged by CMS as "supplies," Apligraf® provides a therapeutic modality to the patient, and is thus much more similar to therapeutic radiopharmaceuticals, which have not been package by CMS. In other words, Apligraf® is not provided in "in support of" a separate and distinct procedure; rather, it is the application of Apligraf® itself that provides the direct therapeutic benefit to the wound.

The primary legal and policy basis for the proposal to package skin substitutes appears to be the agency's analogy to implantable biologicals. With respect to this point the

[30] Id. at 43,571.

[31] 65 Fed. Reg. 18,434, 18,444 (Apr. 7, 2000).

agency states that "We see no reason to distinguish skin substitutes from implantable biologicals for OPPS packaging purposes based on the clinical application of individual products."[32] Critically, again, the agency fails to acknowledge the distinction of SCODs. In the CY 2009 HOPPS Final Rule, CMS used a supply-based policy argument to support packaging three implantable biologics with expiring pass-through status. While these products qualified for pass through payment, they did not qualify for special payment status as SCODs and thus, the statute did not mandate that they be paid separately.[33]

Instead, Apligraf® provides real therapeutic benefits, playing an active role in the healing process by providing the wound with proteins and collagen, both key components in the healing process.

B. Unlike other Skin Substitutes Apligraf® Meets the Definition of a SCOD and Is a Therapeutic Treatment

This legal memorandum only focuses on the authority of the agency to package biologicals like Apligraf® that meet the definition of a SCOD and does not address other skin substitutes that the agency likely has authority to package on policy grounds. With respect to Apligraf®, we would note that it differs from other skin substitutes in both legal and clinical terms. Based on a review of the codes listed in Addendum P for codes to be packaged under this proposal and upon the review of publicly available data, it appears that only one other skin substitute meets the definition of a SCOD.[34]

Additionally, in clinical terms, Apligraf® is different than the other products both based on FDA approved indications and its clinical use as a therapeutic wound healing biological. In the Proposed Rule, CMS refers to a December 18, 2012 report prepared for the Agency for Healthcare Research and Quality (AHRQ) on "Skin Substitutes for Treating Chronic Wounds."[35] CMS points to the report as evidence and support for the proposition that skin substitutes function as supplies and are "not a substitute for a skin graft."[36] However, in the same report, AHRQ specifically distinguishes Apligraf® and Dermagraft® from other skin substitutes, noting in part:

> For these products [Apligraf® and Dermagraft], the term "treatment" is used in the indications for use with chronic wounds. Each of the PMA entries in Table 2 is actually a combination of living human cells and another component (bovine collagen

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[32] 78 Fed. Reg. 43,534, 43,572 (July 19, 2013).

[33] In the FY 2009 Final Rule, CMS packaged three implantable biologics (Neuragen Nerve Guide, NeuraWrap Nerve Protector, and Tissuemend.) 73 Fed. Reg. 68,502, 68,633 (November 18, 2008). All three of these products were first paid on a pass-through basis in FY 2008 and therefore do not qualify as SCODs. See 71 Fed. Reg. 67,960, 68,083 (November 24, 2006.)

[34] See 65 Fed. Reg. 67,798, 67,837 (November 13, 2000) (setting payment rate for Apligraf at $1,157.81). See also 66 Fed. Reg. 59,856, 60,051 (November 30, 2001) (setting payment rate for Dermagraft at $577.60).

[35] AHRQ, "Skin Substitutes for Treating Chronic Wounds Technology Assessment Report," *available a*t http://www.ahrq.gov/research/findings/ta/skinsubs/HCPR0610_skinsubst-final.pdf (Dec. 18, 2012).

[36] 78 Fed. Reg. 43,534, 43,572 (July 19, 2013).

in Apligraf® and polyglactin mesh in Dermagraft®). FDA considers these to be combination products (i.e., combinations of device and biological components into a single entity) and regulates them as medical devices. Besides providing a biologic wound covering, these products also contain human cells capable of producing human growth factors and cytokines that may stimulate angiogenesis, tissue expansion, and re-epithelialization.

The report goes on to state that "[Apligraf® and Dermagraft] have the potential to be interactive with the wound bed and assist in the wound healing process." The report's use of the term "treatment" should be contrasted with the report's use of the word "management" to describe those skin substitutes products considered Class II devices and regulated under the 510(k) process. While a product for the "management" of wounds may be more accurately classified as a supply, products like Apligraf® indicated for the "treatment" of wounds are more accurately classified as therapeutics.

In short, it is both legally and clinically impermissible to group Apligraf® with other skin substitutes as if they were interchangeable. They are not. In the Proposed Rule, CMS describes skin substitutes as "various types of wound dressings" that "stimulate the host to regenerate lost tissue" and that "replace the wound with functional skin."[37] With an uncharacteristic lack of precision, CMS dismisses the substantive distinctions among skin substitutes as their functioning merely "through various mechanisms of action." But it is precisely the substantive differences in these "various mechanisms of action" that distinguish Apligraf® from other skin substitutes. Apligraf® does not function as a supply, cannot be classified as a supply given its special payment status as a SCOD, and thus cannot be paid as a supply.

VI. Principles of Statutory Construction and Administrative Law Prohibit CMS from Altering the Longstanding Treatment of Apligraf®

A. CMS Cannot Change by Regulation a Reimbursement Methodology Established by Statute.

In circumstances where the statute specifies a reimbursement methodology for a given item or service — as is the case with SCODs like Apligraf® — it is settled law that CMS lacks the legal authority to alter that methodology by regulation.

In *Hays v. Sebelius*, 589 F.3d 1279 (D.C. Cir. 2009), CMS contended that the relevant coverage provision of the Act was ambiguous, and that CMS was therefore entitled to deference in its interpretation of that provision. At issue was CMS' contractors' policy of establishing a reimbursement methodology for a multiple-source drug by using its coverage authority. Under that authority, CMS sought to reimburse the drug at the cost of its individual subcomponents. The Appeals Court rejected this contention, concluding that where the Act "unambiguously forecloses that determination [i.e., the Medicare contractor's determination to reimburse for a particular drug only up to the price of its least costly

[37] Id.

alternative]," Medicare must "pay for covered items and services at a statutorily prescribed rate."[38]

Hays placed particular emphasis on the importance of CMS respecting the Act's "mandatory reimbursement formulas," which, in the case of the multiple-source drug at issue in *Hays*, provided that that "'the amount of payment . . . is' 106% of the average sales price, as determined under the statutory formula"[39] (emphasis in original). As explained above, SCODs, too, are subject to a mandatory reimbursement formula under the Act, which provides that the "amount of payment . . . shall be equal . . . to the average acquisition cost for the drug . . . ." Section 1833(t)(14)(A)(iii) (emphasis supplied).[40] *Hays* confirms in no uncertain terms that such mandatory reimbursement formulas must be respected by CMS and implemented as written. "We think it quite unlikely that Congress, having minutely detailed the reimbursement rates for covered items and services, intended that the Secretary could ignore these formulas whenever she determined…".[41]

Finally, the Appeals Court in *Hays* emphasized that while "Congress could have written the Medicare Act to authorize" the policy that CMS proposed, "this is not the statute Congress wrote."[42] There is no dispute that if Congress wished to authorize the packaging of Apligraf® as proposed by CMS in the Proposed Rule, Congress could do so. However, where Congress has established a statutory scheme that singles out SCODs like Apligraf® for distinct treatment, *Hays* reiterates that CMS is precluded from changing by regulation what Congress has required by statute.

B. The Agency Has a Long Standing Policy of Paying Apligraf® Separately as a Biological

There is no discussion in the Proposed Rule of excluding from payment any biological products that meets the definition of a SCOD and payment under the statutory default at ASP plus 6%.[43] As a general principle of administrative law, once an agency "has given its regulation a definitive interpretation, and later significantly revises that interpretation, the agency has in effect amended its rule, something it may not do without

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[38] Hays v. Sebelius, supra n. 11.

[39] Id. at 1,282.

[40] Id. Indeed, CMS concedes that it is statutorily required to reimburse SCODs at AAC. See 78 Fed. Reg. at 43,608, *supra* n. 2.

[41] Hays, 589 F.3d at 1282.

[42] Id. at 1282-83.

[43] In past rulemakings, the agency has packaged diagnostic radiopharmaceuticals that meet the definition of a SCOD. We do not address the issue of diagnostic radiopharmaceuticals as those products are not therapeutics and are ineligible for payment under the statutory default based on ASP plus 6. Section 303(c) of the Medicare Modernization Act of 2003 (MMA) revises the payment methodology for Part B covered drugs that are not paid on a cost or prospective payment basis. Section 303(h) of the MMA excludes payment for radiopharmaceuticals under the ASP methodology and provides for continuation of the payment methodology under Part B prior to the MMA.

notice and comment." *Alaska Professional Hunters Ass'n, Inc. v. FAA*, 177 F.3d 1030, 1034 (D.C. Cir. 1997).

Here, CMS, in 2013, definitively interpreted its regulation as requiring payment for SCODs at the statutory default rate, and it has, since 2001, definitively interpreted payment for Apligraf® separately as a biological. And although the 2014 Proposed Rule contains a recommendation to bundle skin substitutes, it does not solicit public comment on a policy that would exclude from the statutory default biological products that meet the definition of a SCOD, nor does it explicitly propose to cease treating Apligraf® as a biological. Accordingly, we believe that a court could conclude that the public has not been given the effective notice required under the Administrative Procedure Act that the agency is effectively undoing, for at least one SCOD, the policy that it adopted last year and, indeed, re-iterated in this year's Proposed rule. Even more significantly: if CMS adopts its proposed policy as applied to Apligraf®, it will have reversed its longstanding policy of paying for Apligraf® separately as a biological since 2006, without the requisite notice to the public. This is not permissible under the *Alaska Hunters* doctrine.

VII. Conclusion

It is our conclusion that the existing statute is clear and unambiguous: Apligraf® must continue to be paid under the HOPPS payment system as a SCOD, at ASP + 6%. Apligraf® is a SCOD, and the statute, as interpreted by CMS, requires that SCODs be paid at the statutory default of ASP plus 6%. Unlike the other skin substitutes with which Apligraf® would be packaged, Apligraf® is a therapeutic treatment; it is not a supply. Therefore, CMS' rationale for packaging skin substitutes does not apply to Apligraf®. Finally, because the Congress has specified a "minutely detailed" reimbursement rate for SCODs, and because CMS has adopted a longstanding interpretation of the application of that statute, the agency may not alter it, neither under basic principles of statutory construction nor administrative law.

We would be pleased to answer any additional questions that you have regarding our legal analysis.

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Data analysis informing sound policy

TO: Antonio Montecalvo, Organogenesis

FROM: Mary Jo Braid-Forbes

DATE: September 6, 2013

RE: Packaging of Apligraf and Dermagraft

Table 1 below shows the number and percent of times that the costs for Apligraf and Dermagraft are packaged and the average cost per line that is packaged.

Table 1: Number of times Apligraf and Dermagraft get packaged

hcpcs		Total Occurances of Code	Number packaged on 'single' claims	% Packaged	Average Cost Overall	Average Cost when Packaged
Q4101	Aplilgraf	35,409	27,328	77%	$1,159.59	$ 1,154.75
Q4106	Dermagraft	29,287	23,523	80%	$ 936.90	$ 929.27

Table 2 shows when packaged which codes have gotten the costs associated with Apligraf and Dermagraft packaged in. For Apligraf 64% of the time the costs are going to code 15271 and 32% of the time the costs are going to 15275.

Table 2: Codes that Apligraf and Dermagraft are packaged with

			Single claims with any:			
HCPCS	Description	Status Indicator (CMS cost file)	Apligraf Q4101	% of Total Apligraf	Dermagraft Q4106	% of Total Dermagraft
15271	Skin sub graft trnk/arm/leg	T	17,521	64%	2,887	12%
15275	Skin sub graft face/nk/hf/g	T	8,762	32%	19,963	85%
	All other		1,045	4%	673	3%

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Data analysis informing sound policy

Table 3 below shows the costs for 15271 when either Apligraf or Dermgraft is packaged and the costs when these codes are not present on the claim. When Apligraf or Dermagraft is packaged the costs for 15271 are $1,597 compared to only $828 when these codes are not present on the claim. This is entirely accounted for by the higher cost of these products compared to other skin substitutes. The costs reported in the table below are arithmetic means not geometric means.

Table 3: Detail on Costs for 15271 With and Without Apligraf and Dermagraft

	Average Cost		% of Total Cost	
15271 Skin sub graft trnk/arm/leg	NO Apligraf or Dermagraft	WITH Apligraf or Dermagraft	NO Apligraf or Dermagraft	WITH Apligraf or Dermagraft
	16,388	20,408	45%	55%
Total Costs, all lines on claim	***$ 828***	***$ 1,597***	***100%***	***100%***
Items traditionally packaged	***$ 533***	***$ 416***	**64%**	**26%**
Skin Subsititutes	***$ 258***	***$ 1,124***	**31%**	**70%**
Other Newly Packaged	***$ 38***	***$ 58***	**5%**	**4%**