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| First Coast Service Options, Inc.  JN Open Meeting |
| Thursday, August 25, 1 p.m.  Topics:  DL39406– Nerve Stimulators for Chronic Intractable Pain  DL36377 – Skin Substitutes for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers  DL34007-Immune Globulin |
| CORPORATE PARTICIPANTS  Juan Schaening, MD – First Coast Service Options Executive Contractor Medical Director  Alicia Campbell, MD- First Coast Service Options Contractor Medical Director  Laura Mathewson, RN, BSN, CRRN, WCC, CPC-A- First Coast Service Options Medical Policy Nurse  Leslie Stevens, MD- Novitas Executive Contractor Medical Director  Patrick Mann, MD - Novitas Contractor Medical Director  Suzanne Kim Doud Galli, MD, PhD - Novitas Contractor Medical Director  Bradley Davidson, MD - Novitas Contractor Medical Director  Jan Green, RN, MSN, CPC- Novitas Medical Policy Nurse  PRESENTERS  Deborah H. Tracy, MD- JN CAC Member and FL Society of Interventional Pain  Sandeep Patil- Nervo  John Joseph- Medtronic  Robert M. Levy, MD, PhD- International Neuromodulation Society and Anesthesia Pain Care Consultants  Marc Huntoon, MD- SPR Therapeutics  Mehul Desai, MD, MPH- International Spine, Pain & Performance Center  Christopher Gilligan, MD- Brigham & Women’s Spine Center, Brigham & Women’s Hospital  Josh Sandberg- Axolotl Biologix  Aaron Tabor, PHD, CTBS- Axolotl Biologix  Michael J. Schurr, MD- Imbed Biosciences  Francis James-TRUE- See Systems  Christina Dohring- Parametrics Medical  Chris Pittman, MD- Vein911 Clinic  Jeffrey Shapiro- Hyman, Phelps & McNamara PC  Marshall Kevin Medley, DO- BioLab Sciences  Eric Lullove, DPM- West Boca Center for Wound Healing  Marcia Nusgart- Alliance of Wound Care Stakeholders  Karen Ravitz- Coalition of Wound Care Manufacturers  Paul Rudolf, MD, JD- Arnold & Porter, LLP  Jaideep Banerjee, PhD, MSL-BC, BCMAS- Smith & Nephew |

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PRESENTATION

Operator

Good afternoon. My name is Mandy McGarvey, and I will be your Webex host for today's open meeting. Before we get started, I want to take a moment to remind everyone that this meeting is being recorded. At this time, I'm going to go ahead and turn things over to Contractor Medical Director for First Coast, Dr. Juan Schaening. Dr. Schaening?

Dr. Juan Schaening

Thank you, Mandy. Good afternoon. I would like to welcome everyone to First Coast August open meeting. My name is Dr. Juan Schaening. I'm the First Coast executive contractor medical director. Joining me today from First Coast are my colleagues, Dr. Alicia Campbell and Laura Mathewson. Joining us from Novitas are Dr. Leslie Stevens, Dr. Patrick Mann, Dr. Susan Doud Galli, Dr. Bradley Davidson, and Jan Green. Please be aware that First Coast Service Options is recording this virtual open meeting to comply with CMS guidelines. By remaining logged in and connected via telephone or webinar, you acknowledge that you have been made aware that this virtual open meeting is being recorded and you are consenting to the recording. If you do not consent to being recorded, please disconnect from this virtual open meeting. We are holding today's open meeting to discuss the review of the evidence and the rationale for three proposed LCD revisions that are based on LCD consolidations and the development of a new LCD. Open meetings allow interested parties the opportunity to present information and offer comments related to new products and new proposed LCDs and/or the revised portion of a proposed LCD during the 45-day comment period.

The proposed LCDs topics for today's meeting are: nerve stimulations for chronic intractable pain, skin substitutes for the treatment of diabetic foot ulcers and venous leg ulcers, and intravenous immune globulin. During today's meeting, interested party will make presentations of information related to the proposed LCDs. Please remember today's call is being recorded, and we request that all formal comments be submitted in writing before the end of the comment period on September 24, 2022. At this time, I would like to turn it over to Laura Mathewson to provide a brief overview of the proposed LCD nerve stimulators for chronic intractable pain. Laura, please proceed with your review. Thank you.

Laura Mathewson

Thanks, Dr. Schaening. Nerve stimulators for chronic intractable pain is a new LCD. The intent of this LCD is to further define coverage related to NCD 160.7, electrical nerve stimulators, and NCD 160.7.1, assessing patients suitability for electrical nerve stimulation therapy. This is based on our evidentiary review of literature to date. As noted in the IOM 100-03, chapter one, part one, where coverage of an item or service is provided for specified indications or circumstances but is not explicitly excluded for others or where the item or service is not mentioned at all in the centers for Medicare and Medicaid services and NCD manual, the Medicare Administrative Contractor has the discretion to make the coverage decision in consultation with his medical staff and with CMS when appropriate based on the laws, regulations, rulings, and general program instruction.

The new LCD will include the services that are currently addressed in the following LCD. It's L36035, spinal cord stimulation for chronic pain. Therefore, that LCD and its related billing and coding article will be retired when this new LCD becomes effective. Multiple reconsideration requests have been received regarding a variety of electrical nerve stimulation services. There have been significant advances to both the field and published peer-reviewed evidence since the publication of the final core stimulation for chronic pain LCD. Therefore, via this new LCD, First Coast intends to address nerve stimulators, both spinal cord and peripheral nerve, in the context of chronic intractable pain in the Medicare population using current peer-reviewed evidence.

Dr. Juan Schaening

Thank you, Laura. Now let's go to our first presenter it’s the JN CAC Member for Pain Management and CAC member for pain management, Dr. Deborah H. Tracy. Dr. Tracy, please go ahead stating any conflicts of interest.

Dr. Deborah H. Tracy

There are no conflicts of interest for me.

Dr. Juan Schaening

Then proceed with your presentation. Really appreciate it that you're here. Thank you.

Dr. Deborah H. Tracy

Thank you. Good afternoon. My name is Dr. Deborah Tracy. I am a member of the [Carrier?] Advisory Committee for First Coast since 2007. I represent the Florida Society of Interventional Pain Physicians, FSIPP, and its 300 active members as a sub-chapter of the American Society of Interventional Pain Physicians. FSIPP strongly supports the use of spinal cord stimulators and peripheral nerve stimulators as a last resort treatment modality for patients with intractable chronic pain. We provide yearly continuing education with hands-on training workshops and formal didactic sessions on stimulation therapy.

Our shared knowledge demonstrates extraordinary results, and moreover, this treatment, as a non-opioid option, allows us to reduce the epidemic of opioid addiction. Attached to this presentation are 38 citations. I would like to note that a National CMS pain task force was established in approximately 2018 to propose best practices that address gaps or inconsistencies for managing chronic and acute pain between jurisdictions across the country. Consequently, I would first like to address the vast differences between the Noridian LCD A55530, effective date 10/1/21, and the proposed Novitas First Coast LCD DL39406.

The following is a list - and I realize you can't see it - of 54 additional covered indications in the Noridian LCD not found in the Novitas First Coast LCD, which should be included. The extensive complexity in both the pathophysiology and technical aspects of placing stimulators, including amplitude, frequency, pulse duration, and waveforms, primes us to question the data extraction methodology reviewed by the Novitas First Coast jurisdiction and appears to contradict the intention of the task force. We find the Noridian LCD more consistent with concepts that describe and define neuropathic pain. Spinal cord stimulation and peripheral nerve stimulation for refractory pain is considered the standard of care by pain physicians. We strongly request a reconsideration of the covered indications in the Novitas First Coast proposed LCD to also include those that are covered in the Noridian LCD.

There has been extensive literature to support spinal cord stimulation for all the indications of neuralgia, causalgia, RSG, CRPS, and in fact, are covered in the existing LCD. Why was removed is questioned, and we support the inclusion of all causes of neuralgia, causalgia, mononeuropathies. The pathophysiology and mechanism of pain remains the same in each, but the underlying cause of the disease state via direct nerve injury, postherpetic neuralgia, diabetes is irrelevant as the resulting pain and pathophysiology that responds to spinal cord stimulation, peripheral nerve stimulation is treated the same way.

The treatment of refractory low back pain due to degenerative disc disease and discogenic pain is supported by published literature for spinal cord stimulation. The proposed mechanisms of neuropathic pain are similar to central and peripheral sensitization of the lumbar disc and vertebral end plates. In addition, patients who have non-surgical refractory low back pain of any cause have also been shown to improve both pain reduction and functional outcomes with spinal cord stimulation when other treatments have failed. Similarly, cervical and thoracic radiculopathy should be included, not limited to only lumbosacral area. Patients have cervical and thoracic surgery and injuries and have the same exact pathophysiology as if it were in the lumbosacral area. It defies logic to exclude these areas for treatment. Note the most recent studies have shown greater than 80% success in treating pain with spinal cord stimulation and providing greater than 50% pain relief on a long-term basis.

Spinal cord stimulation has been accepted as a treatment for neck and back pain for decades. The proposed mechanism of action, in very simplistic terms, is stimulation of specific nerve fibers, inhibition of excitatory nerve fibers, and inhibition of signal transmission. Peripheral nerve stimulation has gained popularity and effectiveness with the increased use of ultrasound, fluoroscopy to target nerves, the development of secure anchors, and extraordinary evolution in technology. The first recognized research papers regarding peripheral nerve stimulation were published in 1974 and 1976. Through peripheral mechanisms, peripheral nerve stimulation creates disruption of peripheral afferent nociceptive transmission, excitation failure of A-delta and C-fibers, modulating the local biochemical environment by downright regulating local inflammatory mediators, activation of large-diameter sensory fibers, and reduction in ectopic discharges to the central nervous system.

Nerve blocks can help identify that there is mononeuropathic pain, as in causalgia, to determine if peripheral nerve stimulation is a treatment option. Trials are critical to ensure that patients are responding to neuromodulation. We agree with the Novitas First Coast LCD that, quote, "The use of spinal cord stimulation and peripheral nerve stimulation is a late or last resort for pain management after documented failure to pharmacological noninvasive, nonpharmacological management or targeted interventional pain procedures," unquote. We believe that this will decrease the error rate and limit unchained physicians. However, we disagree with the Novitas First Coast limitation section, specifically the use of spinal cord stimulation or peripheral nerve stimulation for any conditions other than those listed in indications, including postherpetic neuralgia, citing reference number 15.

Postherpetic neuralgia is a neuropathic pain syndrome characterized by pain that persists for months to years after resolution of the herpes zoster rash. It stems from damaged peripheral and central neurons that may be a byproduct of the immune inflammatory response accompanying varicella-zoster virus reactivation. The most common location of this condition is following a thoracic dermatome. The lifetime prevalence of herpes zoster is between 20 and 30 percent, rising to 50% by the age of 80 years old. Postherpetic neuralgia or pain after a shingles attack has been estimated to affect 10% of patients who develop shingles but appears to be age dependent. 18% of patients in their 50s had pain for a year or longer after shingles, but the percentage increases 48 for those over 70 and older. Risk factors include autoimmune conditions, rheumatoid arthritis, systemic lupus, inflammatory bowel disease, COPD, depression, diabetes, asthma, lower socioeconomic status, smoking, and other conditions. The patients experience unbearable pain that is constant or intermittent, burning, stabbing, sharp, shooting with hyperalgesia and/or allodynia persisting beyond the healing period of the herpetic rash. In fact, postherpetic neuralgia is one of the most common causes of pain-related suicide in the elderly population.

Other conditions, such as shoulder pain, can also benefit from peripheral nerve stimulation. Current population studies estimate shoulder pain in 18 to 26 percent of patients. Shoulder pain disorders account for one-third of musculoskeletal conditions involving the sensory branch of the suprascapular nerve. Approximately half of patients with acute shoulder pain develop chronic shoulder pain and frozen shoulder. Multiple disease states can play a role. Rotator cuff disorders, tendinopathies, arthritic conditions, adhesive capsulitis, and instability syndromes. Substantial evidence for a role of central sensitization in chronic shoulder pain is prevalent. Pain relief can be achieved with peripheral nerve stimulation to the suprascapular nerve, avoiding the use of spinal cord stimulation. Peripheral nerve stimulation is often indicated when spinal cord stimulation cannot be placed due to systemic coagulopathy, inability to access the epidural space, patient preference, pacemaker, or patient refusal. Additionally, this modality is less invasive than spinal cord stimulation.

Rates of chronic pain at one year after total hip replacement are 38%. The surgical destruction of peripheral nerves and scar overgrowth into nerves leads to permanent nerve damage neuropathic pain. Peripheral nerve stimulation has been an effective treatment for this condition as well as similar preoperative and post-operative conditions for total knee replacement and chronic knee pain. Meralgia paresthetica, a common condition involving innervation of the lateral femoral cutaneous nerve to the anterior lateral portion of the thigh as a result of obesity, pregnancy, pelvic mass, external compression by belts or [inaudible] after laparoscopic surgeries, orthopedic procedures involving the pelvis have an incidence of 32% per 100,000 person years. Success has been reported with peripheral nerve stimulation.

Incidents of brachial plexopathy and upper limb nerve pathologies from upper extremity injuries occur in 3.7% of the population per year. The incidence of direct nerve injury for more uncommon are 0.14 per 1,000. But brachial plexopathies account for 14% of upper extremity nerve lesions due to trauma, such as seatbelt injury after a motor vehicle accident, thoracic outlet syndrome, radiation, and CRPS. We advise that central mediated tracks in the spinal cord and/or peripheral nerves in the human body can suffer from neuropathic pathoanatomy leading to unbearable pain in target areas that does not respond to multiple modalities of treatment. The peripheral nerves affected include, but are not limited to, ulnar, radial, medial, axial, suprascapular, super and middle cluneal, ilioinguinal hypogastric, occipital nerves, cervical sympathetics, intercostal, brachial plexus, sciatic, pudendal, tibial, sural, saphenous, femoral, superior and interior genicular, deep and common peroneal. We agree with the Noridian coverage decision to not support stimulation with fibromyalgia and diffuse polyneuropathy. In summary, ASIPP requests that the Novitas First Coast reevaluate its coverage indications and limitations to allow more alignment with Noridian, expanding the coverage indications, allowing greater patient access to these lifesaving neuromodulation treatments. Thank you very much.

Dr. Juan Schaening

Thank you, Dr. Tracy, for your presentations and for the references provided. That's greatly appreciated. Does any of the CMDs have any questions for Dr. Tracy? Okay. Hearing none. Let's move forward. Before I move forward--

Dr. Leslie Stevens

I'm sorry. I'm sorry. I was [crosstalk].

Dr. Juan Schaening

Oh, go ahead, Dr. Stevens--

Dr. Leslie Stevens

This is Dr. Stevens. Yes. Thank you. I just wanted to take a moment to say thank you to Dr. Deborah Tracy and her commitment as a dedicated CAC member for over 15 years to First Coast. I've been in contact with her in many different policy areas, but she is-- wanted to point out how valued she is to us for-- basically, two features about Dr. Tracy that I think are noteworthy. First of all, she is a tireless patient advocate who is also what I would consider boots on the ground. She has an active practice, and she is very involved with her patients in making sure that they are treated with all of the up-to-date abilities that are out there, technologies. And second, she does also do what we consider a review of the literature and is able to speak-- I shouldn't say speak intelligently, but she's able to speak to the literature and the evidence that supports it. So I just wanted to personally thank Dr. Deborah Tracy for being the CAC member that she is. Thank you.

Dr. Deborah H. Tracy

Thank you, Dr. Stevens. I appreciate that.

Dr. Juan Schaening

And I second Dr. Stevens's comments. Your evidence-based approach to our LCD is greatly appreciated. So moving forward, and something that I also appreciated a lot from Dr. Tracy's presentation is that she kept that within 15 minutes. Due to the amount of presenters, I would like for the other presenters to do the same thing. We have a total of 21 presenters today. So if each person could keep their presentation in the 15-minute threshold, it will be greatly appreciated. So let's move to the second presenter. That is Dr. Caraway from Nevro. Please go ahead stating any conflicts of interest, Dr. Caraway.

Sandeep Patil

Hi, everyone. This is Sandeep Patil from Nevro on behalf of Dr. Caraway, who had some conflicts arise this afternoon. I am a employee of Nevro, and that is my only conflict.

Dr. Juan Schaening

Thank you. Then go ahead, Dr. Sandeep Patil. Thank you.

Sandeep Patil

Thank you. Good afternoon. My name is Sandeep Patil. I'm part of the government affairs and market access team of Nevro Corporation. We are a manufacturer of a spinal cord stimulator that will be affected by the proposed LCD for nerve stimulators for chronic intractable pain. Earlier this year, we submitted a reconsideration request for the current LCD on spinal cord stimulation. Given the FDA approval of our Senza SCS system as the only paresthesia-free solution to treat both painful diabetic neuropathy and non-surgical back pain for those patients with intractable back pain that do not have prior surgery and are not candidates for back surgery. These FDA approvals were based on strong level-one evidence from both our SENZA-PDN and SENZA-NSRBP randomized control trials.

We thank the committee members for their careful review and consideration of our reconsideration request and the clinical data leading to the proposed coverage expansion of both patients with painful diabetic neuropathy and axial low back pain that are refractory to conventional medical management. We also appreciate the committee members' diligence on patient safety, requiring devices to have an FDA-approved indication to treat the covered diagnoses. We believe this is imperative to providing access to evidence-based therapies thoroughly studied for both efficacy and importantly, patient safety. The proposed LCD also has valuable definitions of key terms related to spinal cord stimulation. However, we disagree with the definition of high-frequency stimulation, as stated as greater than 500 hertz. We urge the committee to use a definition of high-frequency stimulation that is consistent with the CMS definition of the therapy that can provide stimulation at 10,000 hertz. We are happy to provide supporting documentation of this definition through the public comment process.

Finally, we ask the committee to consider the real-world practice implications for providers that have patients currently meeting the coverage criteria of the proposed LCD, specifically for painful diabetic neuropathy and axial low back pain, who could possibly be treated prior to the effective date of this new proposed LCD. These are patients that are in debilitating pain who have exhausted all available conservative treatment options, and oftentimes, a delay in patient care can have severe adverse impacts on the patient's function and quality of life. If there's any guidance that can be issued to the provider community in how they should approach these patients and treat these patients, who meet the medical necessity criteria, between now and the effective date of the proposed LCD, it would be greatly appreciated. Again, we thank you for your careful consideration of the published clinical evidence and are available to answer any additional questions as needed. Thank you.

Dr. Juan Schaening

Thank you, Mr. Patil, for your presentation. Does any of the contractor medical directors have any questions for Mr. Patil?

Dr. Leslie Stevens

Hi, Mr. Patil, Dr. Stevens. And I just wanted to make sure that you all submitted through the-- I think you've mentioned that you were going to do that, but I see your summary here, but that if you would please submit your comments and your questions through the formal process. I believe the end date on that is in September. Do you guys remember the--?

Dr. Juan Schaening

September 24 is the--

Dr. Leslie Stevens

24.

Dr. Juan Schaening

--end of the 45-day comment period. So--

Dr. Leslie Stevens

Thank you, Dr. Schaening.

Sandeep Patil

Yes. Absolutely, Dr. Stevens, we do plan on submitting comments before the close of September 24th, the end of the comment period. Thank you.

Dr. Leslie Stevens

Great. Thank you.

Dr. Juan Schaening

Any other comments or questions for Mr. Patil? Okay. Hearing none. Let's move forward. Our next presenter is John Joseph from Medtronic. Please go ahead, stating any conflicts of interest, Mr. Joseph. Thank you.

John Joseph

Yes. Yes, I am an employee of Medtronic, and that is my only conflict. So on behalf of Medtronic and our chief medical officer, Dr. Sharan, I would like to thank the members of the committee for the opportunity to speak with you today. As I said, the name is John Joseph. I am the payer relations manager for Medtronic. While I am sitting in for Dr. Sharan due to a conflict in his schedule, you will have the opportunity to hear from him tomorrow during the Novitas discussion. First, we want to thank the members of the committee for your thoughtful review of our request for reconsideration of the existing LCDs regarding the use of spinal cord stimulation for the new indication of diabetic peripheral neuropathy or DPM.

Typically, DPM presents in patients with a history of poor glycemic control by bilateral pain in the feet and lower legs. This pain, typically stabbing or burning in nature, can progress and lead to numbness that can impair the ability of patients to notice slow-healing sores that can lead to infection and potential limb loss. Before SCS therapy is considered, however, the patient must be refractory to adequate pain control with medication management and non-inceptive therapies. Furthermore, the patient needs to be a good surgical candidate and demonstrate the ability to manage SCS therapy, as well as shows-- as well as show an adequate response to an SCS trial procedure. Having reviewed the proposed LCDs, Medtronic supports your summary as written, that the results from the RCTs reviewed support DPM as an indication for SCS when other appropriate patient selection criteria are met. We further agree with the assessment that the totality of the evidence supports this therapy as clinically efficacious and safe, both conventional or tonic as well as high-frequency systems. We therefore support your coverage of painful diabetic neuropathy that is refractory to conventional medical management and request the inclusion of diabetic polyneuropathy codes E08.42, 09.42, 10.42, 11.42, and 13.42 as proposed, given the evidence.

We did note two other edits in the proposal, not related to DPM, that we want to make the committee aware of. First, there is a proposed change in the dual diagnosis coding. Specifically, the proposed LCAs require a change in the dual diagnosis requirement that Novitas has had in place for many years. What's more, this proposal appears to conflict with ICD-10 official guidelines, which currently align with Novitas and their dual diagnosis requirements. Their current requirement is that claims for SCS must include both a primary diagnosis code indicating the reason for the procedure and a secondary diagnosis code indicating the etiology of the chronic pain. The proposed requirement, however, switches the primary code to etiology and the secondary code to the reason for the procedure. Based on this, we suggest the dual diagnosis requirement language in the proposed LCAs revert to the current Novitas requirement to be in line with ICD-10 official guidelines and to avoid confusion in claims reporting. The second item is peripheral nerve stimulation or PNS. Medtronic is pleased to see that PNS is recognized in the LCDs as there is interest in the clinical community as the evidence and science are still being developed. It appears however that CPT code 64590, insertion or placement of peripheral or gastric neurostimulator, pulse generator, or receiver, may have been inadvertently omitted from the list of applicable codes. This concludes our comments at this time. Again, on behalf of Medtronic, I want to thank the committee for your time and attention.

Dr. Juan Schaening

Thank you for your presentation and for providing it to us in writing. Any additional comments can be submitted up to the deadline of September 24. Are there any questions from the contractor medical directors? Hearing none. I just want to thank, again, Mr. Joseph and move forward to the next presenter. Our next presenter is Dr. Robert Levy from the Anesthesia Pain Care Consultants. Doctor, please go ahead, stating any conflicts of interest.

Dr. Robert Levy

Yes. Hopefully, you can hear me. I am Robert Levy. I am the immediate past president of the International Neuromodulation Society and editor-in-chief of the journal Neuromodulation. While I am appearing on behalf of the INS, as well as Mainstay Medical, I receive no financial reimbursement, nor do I have any equity in the company. Thank you very much for the opportunity to speak to you today about mechanical chronic low back pain that is associated with dysfunction of the multifidus muscles, specifically in the proposed LCD-- oh, wonderful, you have it on screen. Specifically in the proposed LCD 39406 under nerve stimulators for chronic intractable pain, the review and the recommendations appear to follow only peripheral nerve stimulators that are focused on palliative use for pain relief. And we would suggest that a second category, that is peripheral nerve stimulation for rehabilitation therapy, be considered.

That is to say that if we look at peripheral nerve stimulation for rehabilitative or restorative treatment as opposed to the palliative treatment of pain, we see that there are a couple of issues where the guidelines would make it inconsistent with what we think has been overlooked as a peripheral nerve therapy. And the specific issues have to do with the fact that even though this device has been approved by the FDA and is the only treatment that is available for chronic mechanical low back pain after physical therapy and there is a significant amount of evidence supporting medial branch nerve stimulation to treat multifidus dysfunction and secondarily improve chronic low back pain, this is not a palliative therapy; it's a restorative therapy. And the issues really have to do with, one, the inappropriateness of a trial in this setting or having a trial not looking at relief of pain but rather as effective contraction of the multifidus muscle during the implant surgery, and second of all, the fact that it takes time to develop the restoration of this muscular function and is not based simply on pain relief alone.

So peripheral nerve stimulators are typically used as a palliative approach-- next slide, please-- as a palliative approach to neuropathic pain. But there has been a tremendous amount of work over the last 10 years which has possibly escaped attention because the same search words aren't necessarily used. But peripheral nerve stimulation is a treatment to address the underlying cause of mechanical chronic low back pain, which is often a dysfunction of the multifidus muscle, and stimulation of the medial branch nerve for chronic low back pain-- the proposed rules and regulations suggest that the stimulation can only be used or is only properly used for neuropathic pain only, whereas chronic mechanical low back pain is well treated with this restorative surgery and is not necessarily neuropathic.

So who are these patients? Patients who have pain more than half the time, patients who experience their pain for at least a year if not longer. Those have exhausted all conservative measures, including medications, injection therapy, or physical therapy, and where there is no indication for surgery. So these, for example, come from patients-- the MRIs on the right come from patients who were involved in the reactive A/B trial in whom there was clearly no indication for surgery but all of whom suffered from chronic mechanical low back pain. Next slide, please.

What we see on this next slide is a common cause of mechanical low back pain, which is the atrophy and fatty infiltration of the multifidus muscles, and you can see on the right, from the top to the bottom, the increase in white signal within the yellow oval, which indicates fatty deposition and atrophy within the multifidus muscles. This as a diagnosis and a causative method of causing chronic mechanical low back pain has recently been accepted by both Medicare and the CDC, and it has been given a formal ICD-10 diagnostic code, as you see below, which will go into effect on October 1st of this year. Next slide, please.

These are just a list of important references demonstrating the association of chronic mechanical low back pain with multifidus muscle dysfunction and the mechanism under which that occurs. And the references are there for your reference. Next slide. In brief, the pathologic mechanism, is that there is arthrogenic muscle inhibition, so for example, if you have a meniscus injury to your knee, it is often the case that you get deactivation of the quadriceps muscle. Similarly, in the back, when you have patients with a chronic spinal condition, as a secondary response, the multifidus muscle becomes deactivated. The second slide shows that the different signals for central activation of the multifidus muscles on fMRI revert to a general signal when this arthrogenic muscle inhibition occurs, and over time, the process results in those two white comma marks on the bottom of the slide, which is diffuse fatty infiltration of the multifidus muscle, which decreases the support of the back and is a major cause of chronic mechanical back pain. Next slide, please.

What we can see is that there are two ways to clearly diagnose this. One is the prone instability test, which looks at the efficiency and strength of spinal support within the muscles, and secondary is with MRI, looking at the degrees of multifidus muscle infiltration. On the right of the three, you can see severe grade three fatty infiltration, in the middle somewhat lesser, grade two fatty infiltration. Next slide, please. And so as I mentioned, there is an ICD-10-CM code that has been supported by both CMS and the CDC and goes into effect on October 1st. Next slide, please.

And so in summary, currently FDA approved is multifidus muscle stimulation of the dorsal primary ramus of the spinal nerve, which enervates the multifidus muscle, which over time, results in significant and profound reversal of the fatty infiltration and wasting of the multifidus muscle with a large-scale randomized controlled trial that demonstrated the significant efficacy of this in the population of patients, not with the traditional failed back surgery syndrome and chronic neuropathic pain but those with chronic mechanical low back pain. The literature is replete with data. There is a CMS-supported diagnostic code that supports that. And we would look for a dual diagnosis requirement of the multifidus atrophy and fatty infiltration, as well as low back pain or lumbago, and the atrophy and wasting being accompanied by low back pain being the diagnostic criteria for this evaluation.

It is not appropriate to trial for pain response in this setting because the effect occurs over weeks to months and really ceases most maximal effect a year or so after the implant. Patient satisfaction and patient function is significantly improved but doing a trial on the table for pain relief would be inappropriate. And so what we would ask for are the adoption of these diagnostic codes which apply to a restorative therapy rather than a palliative simply pain-relieving procedure. And not only that we have this diagnosis, but the trialing is limited to testing for the appropriate muscular response to stimulation during the trial, and finally, changing the wording so that it applies to a pain that is not neuropathic, as long as these significant requirements are met. Next slide. Yeah, I believe that's it. So, thank you very much for listening to my comments, and if I can answer any questions, I'm happy to do so.

Dr. Juan Schaening

Thank you, Dr. Levy, for your presentation. It's greatly appreciated. Does any of the contractor medical directors have questions for the doctor?

Dr. Leslie Stevens

No, but thank you, Dr. Levy, for your role in the International Society and for speaking at the meeting. We appreciate you.

Dr. Robert Levy

I am honored to hear you say that. Thank you so much.

Dr. Juan Schaening

Okay. Then let's move forward. Our next presenter is Dr. Marc Huntoon from SPR Therapeutics. Please go ahead, stating any conflicts of interest.

Dr. Marc Huntoon

I am Marc Huntoon. I am the director of medical affairs for SPR. So that is my only contraindication, I guess, to speak.

Dr. Juan Schaening

Not a contraindication, just a conflict of interest.

Dr. Marc Huntoon

Yeah, conflict of interest.

Dr. Juan Schaening

All humans have conflicts of interest, so go ahead. [laughter]

Dr. Marc Huntoon

All right. [inaudible] move on to the next slide, please. So I appreciate you allowing me to speak today. So, what I want to go over today is basically characterizing PNS systems, the unique value of PNS treatments and evidence-based outcomes. Next slide. So when we look at PNS systems, in the past, they were generally performed as a trial procedure initially, that a 50% pain relief or greater was met along with some functional improvement might lead to a permanent implantation of a pulse generator with external controls of those devices. The problem with that is that, we believe, based on some recent research, that failed trials may occur, but they may actually underestimate potential opportunities for improvement in some patients. And by the same token, some trials may appear promising during the initial seven-day period, but then later end up not being helpful for the patient. Next slide, please. Thank you.

In some cases, there is no temporary stimulation, which sort of gets back to what Dr. Levy was just talking about. And so the whole paradigm for some of these things is changing, but what we believe is that we probably need to at least consider in some of these patients stimulating the patient longer, and that's exactly what our system is designed to do. It's a 60-day implant, and it, hopefully, and in most cases actually results in long-term pain relief and long-term functional improvement and medication minimization. This is two on the right-hand side. There have been two stimulation [created?], independent RCTs that showed long-term failures of patients that probably were implanted because they had a successful very short-term trial. Next slide, please.

So again, our system is a 60-day-only treatment. There is no trial for it because there is no greater danger in implanting early than doing a nerve block, essentially. It's just a simple needle-directed procedure. Next slide. This is just an example of some of the evidence, and I have expansive knowledge on that. I was editor-in-chief of Regional Anesthesia & Pain Medicine for over seven years. And I just recently gave that up a couple of years ago. But these are looking at a variety of different mechanisms. The LCD differentiates neuropathic pain, but I just want to point out that in the right-hand panel, we have good evidence based RCTs demonstrating improvement in chronic back pain, which is at best a mixed nociceptive and neuropathic pain syndrome, shoulder impingement syndrome, which is clearly a nociceptive pain syndrome, and on the right, post-amputation pain and hemiplegic shoulder pain, both of which could be considered centralized pain syndromes involving the CNS. And I would sort of concur with what Dr. Levy was just saying. We see our therapy as something that we peripherally recondition the central nervous system and are able to affect long-term improvements in patients through that 60-day treatment period, just by that means alone. Next slide.

So, the clinical implications of 60-day PNS treatments are obvious. The patient could have on the left relief that's sustained, and if that's the case, we just watch the patients and see how they do. And we may be able to obviate a permanent implant. If they get no relief, then clearly, we need to consider another therapy because the 60-day treatment period is long enough, in our opinion, in order to see sustained relief. And then if the relief is there but non-sustained, those are the patients that we think probably should be considered for permanent implant. Next slide. I want to show you this, data which is from a recent study looking at 747 patients. And I think two things stand out in this graph. Clearly, the green circles at the top, these are early responders. These patients demonstrated over 70% relief, and that was sustained during the entire 60-day treatment period. Likewise, at the bottom, we have the black squares, and those patients were clearly non-responders, and they stayed non-responders. Could you go to the next slide, please?

I want to draw attention to this middle group though. And this middle group shows two potential responses. One are the delayed responders. These are patients that really didn't cross the threshold until about week three to four, where they moved from being non-responders to responders. These would be patients that would be not implanted because a short-term trial of less than 30 days would not have identified them as being treatment responders. Likewise, we have delayed non-responders. These may be placebo or other mechanisms involved. We're not sure, but certainly, they seem to respond upfront, but then again, by week three or four, they're now non-responders. And here again, these are patients that we would want to not implant a permanent stimulation system in because they're likely to do poorly over time. Next slide, please.

Currently, there are five FDA-cleared PNS systems, and they're listed there. Our company has no permanent implant, and we only have the temporary lead that is treated for 60 days. Some of the companies have both, and some other companies just have either a permanent implant and don't have a temporary lead. Next slide. So when we look at the evidence-based PNS outcomes across pain types, again, we think the neuropathic pain designation is too narrow. We think we've shown through a couple of the recent slides that we can be effective in multiple mechanisms of pain, not just neuropathic. And axial back pain and shoulder pain are two good examples of that. These appear in society based PNS treatment guidelines. One set of that just came out, that I was one of the co-authors for, Strand et al., in August of 2022. Next slide, please.

When we look at peer-reviewed evidence, we also see that there may be painful conditions that are restricted in the new LCD, such as post-cancer pain. And I would submit to you, post-cancer pain-- I've been a cancer pain physician my entire career. There are multiple procedures that are far more involved than doing a simple peripheral nerve stimulator. I think it's overly restrictive for our patients and certainly not patient-centered to not allow them to have some of these things when we would allow celiac plexus neurolytic blocks or other neurolytic procedures, for example, again, which are much more involved. Again, chronic shoulder pain due to impingement, we have good evidence that our device works for that, and clearly, that's not a neuropathic pain condition. Headache and migraine, at least at the minimum, these would be mixed syndromes of both vascular, neuropathic, and muscular etiologies. And we have substantial evidence from the acute post-operative pain realm, with Dr. [Gelfeltz?], multiple studies now, many of which are RCTs looking at outcomes over a variety of different surgical procedures, such as total knee, for example. Next slide.

We want to draw your attention to this. This is real-world data, and this is a poster presentation that's under consideration right now, and I am one of the authors of this as well. But this is nearly 5,000 patients that we looked at our company database. The patients had to give their permission, and their data remained anonymized during the entire treatment period. What we found is - you can see on the right hand in the green bars - we have multiple different types of pain, lumbar medial branches, 1,232. If you move down, we have super scapular and axillary nerves, 564,455. Those would represent treatments for shoulder pain. We have upper extremity treatments, medium, radial, and ulnar. We have ilioinguinal and other groin nerves involved, intercostal nerves. We have cervical medial branches and occipital branches.

So, you can see we're crossing the gamut of multiple different pain conditions and multiple different pain mechanisms. And all of these conditions are showing similar outstanding and very similar quality of pain relief. Next slide. Because of this LCD opportunity to speak, we actually went back and ran the data and compared our outcomes from Medicare-eligible patients. And again, we saw that there's no difference whether the patient is a Medicare-age person or not in terms of these outcomes, once again, across multiple nerve targets and multiple different types of pain pathophysiology. Next slide.

So in summary, we think the LCD is a great first step, but we need to work on the nomenclature. We have to better delineate whether the system is a permanently implanted system, whether it's a treatment, which is what ours is, just a 60-day, one-time treatment only, or whether this is a trial, which would be an implantation for less than 30 days. We believe that PNS treatments greater than or equal to 30 days should precede the implantation of any medically appropriate permanent PNS systems. And we say this because we believe that from that non-responder and late responder data that we can do a better job of identifying these patients. We can prevent delayed responders from advancing, and we can prevent the permanent implantation of PNS systems in delayed non-responders. We do not believe PNS should be restricted to neuropathic pain syndromes, which I hope I've made painfully obvious. And that would be what we have to say on this topic today, and I more than welcome any questions that you would have. Thank you.

Dr. Juan Schaening

Thank you for your presentation. Does any of the contractor medical directors have any questions for the presenter?

Dr. Deborah Tracy

This is Dr. Tracy. I just wanted to emphasize that I didn't think it came apart-- I didn't think it'd come as strongly that the 60-day treatment, after removal of the stimulator, those patients have extended pain release. And that's very exciting in the future for treatment of these conditions. Thank you.

Dr. Marc Huntoon

Yes. Thank you.

Dr. Juan Schaening

Any additional comments?

Dr. Leslie Stevens

Yes. Thank you, Dr. Huntoon, very impressive presentation, and thank you for all your work that you've done in terms of patient care and contributing to release of chronic pain and the suffering associated with it. Thank you.

Dr. Marc Huntoon

Much appreciated. Thank you.

Dr. Juan Schaening

Okay. Then let's move forward to our next presenter. Our next presenter is Dr. Mehul Desai, with the International Spine & Pain Performance Center. Please go ahead, stating any conflicts of interest.

Dr. Mehul Desai

Hi, good afternoon. This is Mehul Desai here in Washington, DC. My conflicts include I'm a consultant for Nalu, and I'm speaking on behalf of Nalu Medical. I also have stock options with SPR Therapeutics, and my organization conducts research that the funds are paid directly to the institution on behalf of Nalu, SPR Therapeutics, and Bioventus Bioness.

Dr. Juan Schaening

Thank you. Go ahead with your presentation.

Dr. Mehul Desai

Thank you very much, and thank you for the opportunity to comment on this draft LCD. I'm going to try not to be overly redundant, and I appreciate the presentations of the folks who came before me. Just a brief statement about the current state of peripheral nerve stimulation. This is a long-established therapy. It's been around for many, many years. Since the 1960s, peripheral nerve stimulation has been used successfully in varying degrees. In over the last several years and especially over the last decade, the success rates have skyrocketed. It's the current standard of care for chronic intractable pain of peripheral nerve origin, both neuropathic and nociceptive, and it's effective in multiple disease states and multiple therapy areas and nerve settings, so extremities such as shoulder, elbow, hip, knee, foot, but also a nerve such as axillary, suprascapular, sciatic, femoral, tibial, just to name a few.

One of the most important things about peripheral nerve stimulation is that we use it primarily in a complex, challenging, heterogeneous patient population. These are folks who oftentimes have no other options, and changing coverage for these folks would be catastrophic. Pain, to some extent, is an N-of-1 disease. So each and every one of these patients are challenging in different and unique ways. And this is a therapy in particular that allows us to customize the therapy for the patient and specifically for the disease state that the patient is suffering from. These are patients who often come in, and they would rather undergo an amputation than to continue to suffer from the pain that they're in. And I'm in a private practice setting here in Washington, DC, so we see patients of a variety of background and a variety of disease states. And we see this over and over again, that these patients are desperate for help and desperate for options.

There's been an NCD in place, NCD 160.7, since July of 1988, via transmittal number 26, which is established coverage for peripheral nerve stimulation. So changing some of the items on the draft LCD would really significantly alter coverage for patients. Can't reiterate enough that this is a minimally invasive therapy that's reversible. It's opioid sparing, and oftentimes, if this wasn't an option for patients, the only thing they could do was to be on opioids. As an example, patients who have post-stroke shoulder pain or non-surgical shoulder pain from osteoarthritis, their only option, oftentimes, is to be on medications and to stay on medications for the rest of their lives. And for these patients to be offered an option that could help them avoid opioids can be life changing.

Another thing to emphasize is this is one of the few things in medicine where patients can trial it first. So that also provides a barrier to sort of unrestricted expenditure. So the ability to try stimulation prior to permanent implantation allows both to weed out patients who may not be good candidates, but also to give patients an opportunity to understand better what the therapy is and to determine if the therapy is right for them. And as such, there are going to be patients that don't move on to permanent implantation, which can help us limit expenditure in this case. There are decades of clinical research and outcomes that have helped establish peripheral nerve stimulation as a standard of care, and I'm going to talk, in a few slides, about the multiple new PNS trials that are underway. And again, these trials are across a variety of therapy areas and use cases. And again, this emphasizes the idea that this is a heterogeneous patient population. And one of the major challenges we've admittedly faced is studying heterogeneous patient populations, especially those who are difficult to treat because of the variability in how the diseases affect them, continues to make these therapies challenging to study despite robust, established patient benefit and the fact that physicians are successfully using these devices all the time. Next slide, please.

This was mentioned earlier, but it's an important point from our perspective, which is that it feels like it's a potential oversight that CPT code 64590 was excluded from the proposed LCD. 64590 is insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling. Traditional peripheral nerve stimulation requires implantation of a pulse generator. And as such, CPT code 64590 would be necessary for those devices to be used. And again, can't emphasize enough that this code would be very important to place back on onto the LCD. Next slide, please.

One of the things wanted to emphasize was that the Pain Management Best Practices Inter-Agency Task Force, which was convened by HSS in 2018 in conjunction with the DOD, the VA, and the ONDCP, was intended to put forth an identification of the gaps, inconsistencies, and updates to make recommendations for best practices for managing acute and chronic pain. And this proposed LCD appears to be in direct opposition to that HSS task force, where consistency is an important part and an important conclusion from that, where would now be significant differences between, for example, the Noridian LCD and the Novitas LCD or the FCCO LCD in this case. Next slide, please.

There are more comprehensive coverage policies. Specifically, the Noridian LCD has a significantly larger list of covered disease states, and I believe our last slide talks a little bit more about those disease states. The Noridian LCD, which is L34328, has been in effect, and the most active LCD is L37360. And this more comprehensive disease state accounts for, again, the variability amongst patients in terms of the huge spectrum of disease states that they're suffering from. There is clinical evidence, new clinical guidelines, and review papers further strengthen the case for broader application for PNS. Some of these are also mentioned and are also cited in our presentation here.

There's now a considerable body of clinical literature supporting peripheral nerve stimulation and using it even beyond the highlighted clinical reviews. One of the things that's happening is that the amount of evidence that's coming out into the public domain is far outstripping our ability to review it, so for every review paper that comes out, there's already a multitude of studies that have been published that sort of continue to push the test use. Current and active clinical studies will only serve to further strengthen and shore up available literature. So, one of the requests we would make is that additional diagnoses be added back to the current draft LCD. Those would include the diagnoses that apply to peripheral nerve stimulation for mononeuropathies both of the extremities and of the trunk, as well as peripheral nerve stimulation for CRPS type 1 and type 2 and causalgia as isolated to one major peripheral nerve. Next slide, please.

This is just sort of the next several slides or additional citations as they apply. And this is intended to highlight the fact that there are numerous citations that address each and every one of the diagnosis codes that we've requested be added back to the draft LCD. So, we've got peripheral nerve stimulation for upper extremities, so mononeuropathies of the extremity in trunk and the upper extremities, which we've got 10 citations here. Next slide, please. Peripheral nerve stimulation with mononeuropathies of lower extremities. We've got an additional 9 to 10 citations on this slide. Next slide, please. And then, as it pertains to the trunk, there's also a battery of data that's available for review that supports use in the trunk. Next slide. And as far as peripheral nerve stimulation for CRPS and causalgia isolated to one major peripheral nerve, there are also a series of studies that have been published that address this disease state. Next slide, please.

One of the things we wanted to highlight is that there are a host of clinical trials currently ongoing. Even a cursory look on clinicaltrials.gov finds that there are 20 PNS RCTs that have been recently completed or are ongoing currently, representing 1,500 subjects. So, there is a commitment on the part of physicians and industry to continue to invest in clinical trials that look at and examine peripheral nerve stimulation and to continue to publish clinical trials that look at outcomes as they represent the experience of the folks going through these clinical trials. Next slide, please. In this last slide is, again, a recommended list of additional diagnostic codes that we would request would be added back to the draft LCD, including those that focus on mononeuropathies, those that focus on causalgia, and those that focus on complex regional pain syndrome. Thank you again for the opportunity to comment on this draft LCD. I'm happy to take any questions.

Dr. Juan Schaening

Thank you so much. Are there any questions for the presenter?

Dr. Leslie Stevens

No. But again, I'd like to thank you, Dr. Desai, for all your work in this arena and for sharing all of the references and certainly the up-and-coming research that's ongoing. And it's nice to see continued excellent research to help define the proper indications for implantation. So thank you, again, for the presentation.

Dr. Mehul Desai

Thank you. Thank you so much.

Dr. Juan Schaening

Okay. Any further comments? Hearing none. Let's move forward to our next presenter. Our next presenter is Dr. Christopher Gilligan from Brigham and Women's Hospital. Please go ahead, stating any conflicts of interest.

Dr. Christopher Gilligan

Thank you. Good afternoon. My conflict is that I do serve as a consultant for Mainstay Medical, and I'd like to take a moment to thank the committee for the chance to present to you and also for the diligent and thoughtful work on the LCD. I'm going to speak about ReActiv8, which is a peripheral neurostimulator targeting the medial branch nerve, with restorative neurostimulation for the management of chronic low back pain. Next slide, please. So the reason that we're so dedicated to treating this therapy-- the reason that I have focused a lot of my research on treating this condition is that chronic low back pain is a leading cause if not the leading cause of years lived with disability worldwide, and we think that disability is, of course, relevant to Medicare. It's often a determinant for chronic opioid use. It's a major driver of both direct and indirect costs to society. And for a very large number of patients, mechanical chronic low back pain is correlated to multifidus dysfunction. The previous or current treatments that are available to these patients are far too often ineffective or provide only transient relief. And the prognosis for these patients, once they're chronic and their pain is persistent for one year, two years etc., or even more, is unfavorable. The natural history is not that they're going to recover on their own without an effective therapy. Next slide, please.

So, on the left is radicular neuropathic pain often seen in the setting of failed back surgery, surgery maybe indicated for some of these patients, and that's treated with some of what we've been talking about, palliative treatments, spinal cord stimulation, as well as peripheral nerve stimulators that target sensory innervation. Those leads work for conventional spinal cord stimulators or, of course, in the spinal canal as shown on the radiograph to the lower left. What I want to talk to you about is treating mechanical chronic low back pain, which can be due to impaired muscle control of the multifidus. Dr. Levy spoke earlier about the role of the multifidus as the strongest stabilizer of the lumbar spine. And again, these patients have few therapeutic options. For the vast majority of these patients’ surgery is not indicated, and opioid treatment remains fairly common.

What we're doing with this therapy is we're stimulating the medial branch nerve, which is the motor innervation of the multifidus muscle, and whereas as the other therapies that have been discussed today and that we use in this field are typically restorative-- excuse me, are palliative treatments targeting sensory nerves, this is a restorative treatment. This is restoring function of the multifidus muscle in order to restore neuromuscular control and functional spinal stability such that the patient doesn't have pain. But it's not palliative. It's not covering up the pain by stimulating sensory nerve. As you can see on the radiograph on the lower right, the leads for this are outside of the spinal canal. Next slide, please.

So, this is what the system looks like in an anatomic drawing. The patients are using this for 30 minutes twice a day. Typically, 30 minutes before they get out of bed in the morning, 30 minutes before they go to sleep, in bed in the evening. And again, we're using it to override the inhibition of the multifidus. We are [lessening?] afferent sensory input. And in this way, we're restoring the neuromuscular control of the multifidus muscle such that we restore functional spinal stability, and the patient's pain is resolved. Next slide. This device is FDA approved through a pre-market approval. It's a known implant technique and a known anatomical target, namely the bilateral L2 medial branch nerves. The electrodes are placed, as I mentioned, outside the spinal canal. And it's patient-controlled therapy sessions 30 minutes, twice daily. Again, we're invoking a rehabilitative mechanism aimed at restoring multifidus neuromuscular control and lumbar spine stability. Next slide, please.

These are some of the clinical trials and the associated publications. I'm going to focus here on the ReActiv8 B trial, which was our pivotal trial that resulted in that FDA approval. Next slide. That trial was 204 patients at centers around the world. Their age range was 22 to 75 years for our patients. On average, they had 14 years of low back pain and pain 97% of the days in the prior year. 100% of our patients had failed physical therapy. On average, they had been to 31 sessions. 100% had failed pain medications. 37% were on opioids at baseline, and 52% had failed interventional pain therapy, such as radiofrequency ablations and epidural steroid injections. Key exclusion criteria were prior low back surgery or any current indication for low back surgery, and all of these patients were reviewed; their cases were reviewed by an experienced spine surgeon to make sure they did not have a current indication for surgery. They also couldn't have leg pain greater than back pain; we didn't want patients with a neuropathic genesis to their pain.

So, if you look at the graphic on the right, that red dot shows where our patients started on average. On average, they had baseline pain, baseline VAS of 7.3 centimeters - that's severe pain - and a baseline Oswestry Disability Index of 39 points. That's right where moderate meets severe disability. Next slide, please. So this slide is showing the percent change in their pain over the course of three years of stimulation, 36 months of stimulation. The solid green line is patients who were on therapeutic stimulation from the beginning of the trial. The red line is patients who were on sham stimulation for the first 120 days of the trial, and then after 120 days, those patients were crossed over to therapeutic stimulation, and that's where you see a dashed green line. I think there are three takeaways from this slide. There's a significant initial sham response. And after we cross those patients over to therapeutic stimulation, there's a catchup affect. And I think the most important thing that we see here is a progressive long-term improvement for these patients. The longer we treat them, the better they do. Next slide, please.

On this slide, we're looking at pain on the left, Oswestry Disability Index in the middle, and healthcare-related quality of life, the EQ-5D, on the right, through 36 months of stimulation. So if we start with pain, our patients started on average with pain of 7.3. And after 36 months of stimulation, their pain was 2.4. Many people will call anything less than 2.5 a low back pain [meter?]. Their Oswestry Disability Index started at 39.1, and after 36 months of stimulation, it was 16.4. Anything less than 20 on the Oswestry Disability Index is mild disability. And after 36 months of stimulation, on average, our patients had an EQ-5D of 0.85. That's very close to the US population norm for healthcare-related quality of life measured by the EQ-5D. Now, importantly, a trial does not have a clinical role for this restorative stimulation, not a 7-to-10-day trial, not a 60-day trial, because it's a restorative mechanism of action where it takes weeks and in some cases months to restore the function of the multifidus and restore that neuromuscular control. Next slide, please.

This is the same data that I just showed you except that on the previous slide, I showed you the patients who completed 36 months of stimulation. That's still here on the light green, for pain on the left, disability in the middle, and healthcare-related quality of life on the right. Here I just added in the imputation for it to account for all 204 patients. That's what's in the dark green. And what you can see is that even using an extremely conservative imputation to account for all 204 patients, the results remain essentially equally impressive. The longer we treat these patients, the better they do in terms of their pain, their disability, and their healthcare-related quality of life. And after 36 months their pain is mild, their disability is mild, and their healthcare-related quality of life is approaching the US population norm. Next slide, please. Let's look at the responder proportions at three years. 85% of our patients had substantial improvements - that's 50% or greater improvement - in their pain and/or their disability after 36 months of stimulation. And 59% of our patients had substantial improvements, 50% or better improvements in both their pain and their disability after 36 months of stimulation. In terms of opioids, 71% of our patients on opioids at baseline voluntarily eliminated-- or that was 49% or reduced their intake, 22%. And that was entirely voluntary. Next slide, please.

Here I'm shifting from that ReActiv8 B trial to two other trials very quickly. The top one is a real-world trial that Simon Thompson and colleagues conducted and published from the United Kingdom, showing that through two years, [whether we're looking at year?], both pain and disability continue to improve. The longer we treat these patients, the better they do. And that's in a real-world population, not a clinical trial population. And then the bottom two panels are an earlier trial that we did that has four-year data. So there we're looking at four-year data from a different trial, showing both pain and disability continue to improve. The longer we treat these patients, the better they do. So we've seen it in our largest pivotal trial but also in a real-world trial and also through four years in an earlier trial. Next slide, please.

I talked a lot about the efficacy of this therapy. I want to take a moment to look at complications. The white columns are published averages for complications from spinal cord stimulators from Salim Hayek and Sam Eldabe. And then the green is what we saw in our trial. So we saw a 3% infection rate, 8% implant site discomfort, 3.9% lead fracture or malfunction. Importantly, we saw 0% lead migration rate, and lead migration is often cited as the most common complication of spinal cord simulators. 31% of our patients needed a surgical intervention. 22% it was a system explant for infection, need for MRI, inadequate pain relief, or resolution of pain thanks to the therapy. 5.8% needed a lead replacement. Next slide, please.

So, in terms of the proposed LCD, we feel that mechanical chronic low back pain associated with multifidus dysfunction historically had really no good treatment options. The treatment options that existed were palliative only, the Septra injections, radiofrequency ablation, opioids. Robust data supports the correlation of mechanical chronic low back pain with multifidus dysfunction, and Dr. Levy also covered some of that. And now we have a treatment available to solve the underlying cause, namely this restorative stimulation. Medial branch nerve stimulation with this therapy, ReActiv8, is well studied for this indication, and we feel it should be included for coverage that is akin to the neuropathic pain coverage. A trial for peripheral nerve stimulation therapy should take the form here for this restorative stimulation of documenting the physiologic response while the patient is on the operating room table and we can we see the contraction of the multifidus before an implantable pulse generator is implanted. Next slide, please. And here I just included some citations that we feel are very relevant to this topic. And with that, I thank the committee for the opportunity to present, and I would be delighted to take any questions or comments. Thank you.

Dr. Juan Schaening

Thank you for your presentation. Are there any comments or questions for the presenter? Again, we appreciate your time and your commitment to our patients. Hearing none. Let's forward. There are no further presenters for this local coverage determination, so we're going then to move forward with our presentation for the next LCD. I would like to turn it over to Jan Green to provide a brief overview of the proposed LCD, skin substitutes for the treatment of diabetic foot ulcers and venous leg ulcers. Ms. Green, go ahead.

Jan Green

Thank you, Dr. Schaening, and good afternoon, everyone. This LCD has been revised to create a uniform LCD with other MAC jurisdictions. Once this revision to the LCD becomes effective, the current First Coast LCD L36377, application of skin substitute grafts for treatment of DFU and VLU of lower extremities, and the related billing and coding article A576AM will be replaced with this revised policy. This LCD provides coverage for skin substitute graft products, meeting the necessary FDA regulatory requirements of skin replacement surgery for wound care of diabetic foot ulcers and venous leg ulcers. The proposed LCD and associated billing and coding article are being reposted to add language to the analysis of evidence section of the LCD, recommending that the manufacturer of particular skin substitute grafts or CTP products obtain the appropriate regulatory information and evidence-based literature, if available, and send it to the MAC.

Once this information has been received by the MAC, the products will be considered for coverage and placed into the appropriate code group and the related billing and coding article. The documentation requirements section of the related billing and coding article has been revised to move the satisfactory evidence of FDA regulatory requirements to a separate paragraph and to move several HCPCS codes in the CPT HCPCS codes section or group two codes to the group three codes-- the group three codes, excuse me, non-covered, due to lack of evidence to support coverage. The comments that have already been submitted are continuing to be reviewed, and these comments will be addressed in the response to comments or RTC article posted upon finalization of the LCD. Therefore, please, limit comments for the reposted LCD and article to the changes made in the reposted documents. Back to you, Dr. Schaening.

Dr. Juan Schaening

Thank you for your presentation, Jan. Let's move forward with our first presenter. Before we do that, we have 12 presenters, so let's limit the presentations to 15 minutes if-- that's 15 minutes, and they're repeat presenters from the previous open meeting. They can be assured that their comments will be addressed on the comment response document, so there's no reason to repeat their previous comments. So let's move forward with the first presenter that is from Axolotl Biologix. Their presenters are Dr. Aaron Tabor, Dr. Gary Jones, and Josh Sandberg. Please go ahead with your presentation and stating any conflicts of interest.

Josh Sandberg

[Thank you?] for your time and opportunity to comment on this LCD on behalf of our company and technology. We can go ahead and move to the next slide. And even the next one. The presenters. My name is Josh Sandberg, and I'm the chief strategy officer for Axolotl Biologix and have been with the company since April of 2019. Along with me in the presentation today will be Dr. Aaron Tabor, who has been with the company also since 2019 and has a PhD in biological sciences. Dr. Gary Jones, a cardiothoracic surgeon, wanted to join us to share his experience using Axolotl DualGraft, but he is currently held up in the operating room and cannot make the call. But he has expressed an interest in submitting his thoughts in a subsequent communication. Next slide, please.

Axolotl Biologix was founded in 2016, based on disruptive science that was originally discovered in the late 1990s by Dr. Robert Keller, our chief science officer. We are an IP-focused company that strongly desires to work with regulators like the FDA and CMS to bring the most safe and effective products to the market for our clinician partners and ultimately the patients we serve. One example of this is our non-commercial suspension products, which we're currently enrolling patients in for our phase one, phase two IND clinical trial. We're not discussing that in this as it relates to this LCD, but just wanted to share the product portfolio that we have. We're proud to share that we do a quality system-focused sales organization that spans 44 states, and our products have treated patients from over 125 different payers. Next slide. We are supportive of an LCD that clearly defines requirements of care related to DFU and VFU treatments. We also recognize that this list was created based on information at the time of publication. Therefore, based on some new information we will present, we are appealing to the group for reconsideration of our current position in group three to be moved into group two, and we have reasons that Dr. Tabor will now discuss in the subsequent slides.

Dr. Aaron Tabor

Thank you, Josh. And thank you to the members of the panel and for those of us who are joining today. The slide here details an ongoing trend that we're seeing at the global level. We know that diabetes, as it's correlated to increasing obesity rates, impacts many people at the global scale, including those in our country. To date, there are correlated events that lead to diabetic foot ulcers and venous leg ulcers that are also rising in numbers and subsequent cost. With that, treatments such as skin substitute therapeutics must be implemented and provided to these patients in need. Those treatments must be safe and effective and administered by qualified physicians while properly regulated. One product that falls into this category is the Axolotl Graft and DualGraft products. Next slide, please.

The Axolotl DualGraft products, as we're speaking to this LCD update, are manufactured in an American Association of Tissue Banks-accredited facility located in Phoenix, Arizona. These are terminally irradiated products with a SAL level 10 to the minus 6. They're solely marketed under section 361 of PHS Act and regulated under 21 CFR part 1271. Axolotl Biologix is registered through the FDA's Center for Biologics, CBER. These grafts or skin substitutes are indicated as a wound covering and act as a barrier. To date, Axolotl has six acellular dehydrated graft products varying in sizes that aid in these patients' need. Next slide, please.

As Josh, our chief strategist, alluded to, we have recently had positive feedback from the FDA's Tissue Reference Group as required as part of these LCD updates. Prior to the posting, in April of this year, Axolotl Biologix submitted a request to the executive secretary of the Tissue Reference Group at the FDA for guidance and a recommendation to be solely regulated under 361 of the Public Health and Safety Act regulations and part of 1271. Subsequently, early August of this year, August 3rd, we were positively received by the executive secretary of the FDA and have subsequently received this sole regulation as a 361 regulated under 1271 product. Next slide, please.

To date, Axolotl is currently undergoing many efficacy studies and R&D research as it relates to these grafts. Axolotl has been accepted this fall to the Symposium on Advanced Wound Care, as we are exploring the mechanical and biological characterization properties of the Axolotl DualGraft. Additionally, we are looking at a retrospective study with the Axolotl DualGraft being a tissue-based wound covering and barrier product. Beginning 2023, we are looking at a multi-site randomized study using the Axolotl DualGraft as part of the requirements listed herein. Next slide, please.

In conclusion, Axolotl is requesting to be removed, as Josh stated, from group three to a favorable group as being included in the new evidence that is supported that we are solely regulated under 361, 21 CFR part 1271 with the FDA. We have received the letter, as demonstrated, item number two for skin substitute grafts or CPTs, classified as human cell tissue and cellular tissue-based products, HCT/Ps. A letter from the FDA indicating that the HCT/P has met regulatory guidance is acceptable evidence. Axolotl Biologix has received that letter in support demonstrating this. Next slide, please. In conclusion, we would like to thank the participants today, those who have attended, and at this point, we will welcome any questions.

Dr. Juan Schaening

This is Dr. Schaening. I appreciate your presentation. Does any of the other CMDs have a comment or a question for the presenter? Okay. Hearing none. I will make a comment myself. We really appreciate your presentation. The intent of this reposting of this LCD is to provide manufacturers that opportunity to give us their regulatory evidence in addition to clinical evidence of the reasonable and necessary use of this as a skin substitute graft. We really appreciate that you included the Tissue Reference Group, a letter that provides you evidence that you are regulated under 361 when used for the homologous use as a barrier of a covering. We will appreciate that any additional clinical published literature can also be provided that applies to your product and all the products. That was the intent of this additional comment period; we want to receive all those Tissue Reference Group letters and all the additional published clinical evidence to support the effectiveness of these skin substitutes grafts or human cell tissue products as one treatment in wound care of these ulcers. So no further comments on my part. We really appreciate your comments. I just wanted to emphasize that before we move to the next presenter. Okay?

Dr. Aaron Tabor

Yes, sir. We will be submitting that during the public comment period prior to the closure of the 24th.

Dr. Juan Schaening

Greatly appreciate it. Let's move to our next presenter then. It's Dr. Michael Schurr from Imbed Biosciences. Please go ahead, stating any conflict of interest.

Michael Schurr: 01:31:53 Good afternoon, everybody. I just want to make sure you can hear me.

Dr. Juan Schaening

Loud and clear. Proceed.

Dr. Michael Schurr

Right. Thank you. So I'm Dr. Michael Schurr. I'm the chief medical officer and also founder of Imbed Biosciences. I'm the chair of surgery at MAHEC, and I'm a general trauma/burn surgeon here in Asheville, North Carolina. I'd like to thank you, the panel, for the opportunity for spending the time with us this afternoon and would really like to bring everybody up to speed on Microlyte Matrix, which is a synthetic antimicrobial skin substitute that is just sort of newly out on the market, to update you with our data and our clinical efficacy. So the objectives of this talk provide the background information on the Microlyte Matrix, which has been approved for reimbursement, 82005 code, discuss sort of the regulatory approval process from the FDA and the instructions for use for the product, discuss some of the clinical evidence for the management of VLUs and DFUs, and really what we'd like to do is request LCD coverage as a new and novel synthetic antimicrobial skin substitute. Next slide.

So really, our core technology hinges around polyelectrolytes, and polyelectrolytes are very friendly compounds. They're thought to be-- they're widely used in medicine. They're really well thought of from a FDA and approval perspective. These are abundant in nature. They recreate a physiologic wound environment. There are inherent antimicrobial properties. They recreate extracellular matrix and stimulate growth factors in macrophages in growth and into wounds. And so that's the background of our technology. Next slide.

What we've been able to do is take these polyelectrolytes and create a multilayer matrix. So we create a 15-layer polyelectrolyte matrix. We have a three-dimensional structure, and we can then use this structure to add antimicrobial agents. And like some of the other presenters today, this is a core technology. We're a pipeline company and have additional products working through the FDA as we speak. Next slide. And what we create here is we create this multilayer matrix loaded with silver. And our silver is all on the size of 7 to 10 nanometer and molecules of silver, which are extremely effective in terms of antimicrobial activity. In addition to three-dimensional matrix here is a substrate for human cell growth. And we've shown very clearly that human cells love to grow on the surface of the skin substitute. We've shown that we've accelerated wound healing in multiple different animal models, including infected and non-infected animal models. Next slide.

So, we're very unique here in that we're completely synthetic. We don't have any animal or human components. We are also unique in that we're a skin substitute, but we're antimicrobial, and our antimicrobial efficacy is very high. We kill 99.99% of all the important pathogens, the staph aureus, MRSA, VRE, pseudomonas, E. coli, klebsiella. We kill candida species, and we actually also show that we kill viruses. And as everybody knows that antimicrobial burden of VF use and venous stasis ulcers is one of that, the major components that impairs the healing process, and having a skin substitute with these antimicrobial properties is going to be very important to the patients, and we've shown that clinically. Next slide.

So we have a published prospective clinical trial. This was done by an independent investigator, so this was not a company-funded trial. This was an independent investigator that had worked with the Microlyte Matrix skin substitute, really believed in the product. He did an IRB-approved prospective evaluation, and these were all patients in his clinic. And at baseline, these were non-healing for an average of 40 weeks. And what he showed is that 72% of these patients with chronic wounds had an average closure of two-thirds, 66% closure of these wounds after only three weeks of therapy. That is well above the bar of 50% closure at four weeks, so we're really proud of this data. We're proud of the fact that we've got published data to support our animal data. And I just have some representative cases. Next slide.

This is just to really show the skin substitute in use, and you can see this is just an after-lunch-appropriate venous stasis ulcer with the Microlyte Matrix skin substitute on the top of it. And you can see it really creates a intact matrix on the wound. When it's placed, it's properly affixed to the skin. Next slide. And this is another case. This is really heroic save of a necrotizing soft tissue infection almost in a diabetic foot. Patient came in with a diabetic foot ulcer that was untreated. Had to have radical debridement of his foot. He was treated with the Microlyte Matrix skin substitute, and you can see on the bottom right-- I mean, that's not the world's best foot, but he's got complete closure. His foot is saved and intact, and he can get up and ambulate and really engage in his own activities of daily living because we did manage to salvage his foot. Next slide.

This is a little bit out of the realm of DFUs and VLUs, but I think this is an important case because it brings in a lot of what we're finding clinically. This is an elderly man who had cutaneous cancers on his scalp. Was treated with Mohs surgery and then radiation. Plastic surgeon called from some place in Philadelphia. Called our office and said, "Can you do anything for this man? He's been in my office three times a week for the last month. He's in terrible 10-out-of-10 pain. It takes four hours to do the dressing change because he has such terrible pain, and we've had no resolution of this wound." He had the Microlyte Matrix placed. You can see day 1A and day 1B. Immediately, his pain went from one month of a 10-out-of-10 pain to a 4-out-of-10 pain, with one application of the skin substitute. After four days of treatment, the patient's wound size decreased by 42%. So here is a patient who is miserable for an entire month, with terrible pain. The Microlyte Matrix skin substitute was used with pain control, but amazing efficacy in terms of wound closure. Next slide. So we are on the market. We are FDA approved, 510(k). We're approved for all wounds, partial thickness wounds, including partial ulcers, venous stasis, diabetic foot ulcers, and you can see the rest. Next slide.

So, I'd just like to conclude and see if there's any questions. We are a newer company. We're a start-up. We're very excited about our Microlyte Matrix skin substitute. It's A2005. I think this is a medically necessary skin substitute. It's completely synthetic. There's no human or animal components, which gets away from some of the issues that are in the field. It's placed as a graft and affixed to the surrounding skin. The three-dimensional matrix is very important here. It recreates a physiologic wound environment, and it supports human cell growth. We've shown that in vitro, we've shown that in vivo in several animal models, and we've shown that in prospective published clinical trials in patients. We're unique and novel that we have five-to-seven-nanometer silver particles that have amazing kill of resistant organisms. Like I said, we accelerate wound healing, and we're requesting medical coverage under the LCD as a medically reasonable and necessary skin substitute. And we would like to thank everybody for their time. I know how these work. That's long days. But thank you for listening, and I'm more than happy to answer any questions.

Dr. Juan Schaening

Thank you for your very interesting presentation. I have no questions for my part. Does any of the other contractor medical directors have questions for the presenter? Hearing none. I want to thank him again. And as I had told the other presenters, I have the [inaudible] number. We have access to that letter. But any additional clinical literature that they can provide, it will be welcome.

Dr. Michael Schurr

Yes. We will do that.

Dr. Juan Schaening

Thank you.

Dr. Michael Schurr

Thank you very--

Dr. Juan Schaening

So--

Dr. Michael Schurr

--much.

Dr. Juan Schaening

--let's move forward then to the next presenter.

Francis James

Hi. This is Francis James with TRUE-See. Does everyone hear me fine?

Dr. Juan Schaening

We can hear you very well. So Francis James, please proceed, stating any conflicts of interest, and you can go ahead and do your presentation.

Francis James

I don't have any conflicts of interest regarding skin substitutes. We do wound care photography and measurements in other EMRs. We're embedded in EMRs, but we don't directly deal with wound substitutes. So I just wanted to-- I guess we can go to the next slide, introduce myself. I'm Francis James. I'm a little bit of an anomaly. I am the founder and CEO of TRUE-See Systems. I'm also a cinematographer in the International Cinematographers union. And one of the things that I've seen from going back and forth between the two worlds is the real need for quality and integrity in photographs and photo documentation. Go to the next slide. Will be focusing primarily not specifically on skin substitutes, but the support of them. And I want to thank you, First Coast - [inaudible] the slides for tomorrow as well - for this opportunity to speak to everyone. And I know this is a really important problem to solve, and I really appreciate all the great work, particularly of other co-presenters and clinicians, skin substitute producers.

I've been in many clinics, and this is a really critical population to provide relief for. So I thank you for the opportunity. What we'd like to do is seek to improve patient care by enhancing the integrity and measurable quality of the photo documentation that informs and supports that care, so we see ourselves in more of a supporting role than the others on this call, both clinicians and producers. Go to the next one. Next slide. No, one back. There we go.

So photo documentation is an integral part in the medical record. And the physicians rely on it for wound assessment and treatment and evaluation, and such is a medical necessity in appropriate use of skin substitutes for the treatment of diabetic foot ulcers and venous leg ulcers. Specifically, photo documentation requirements would greatly enhance the evidence and provide an alignment of permits with the best practice of wound care. One of the things that we see here is that in the draft articles, the requirement for documentation states that the submitted medical record must support the use of the selected ICD-10 code. And to subscribe that service provided in the medical record, documentation must support the medical necessity of skin replacements. So the support of these documentations is where I'm focused on because this appears to disregard the role of photo documentation as a part of the medical record when you read further into these requirements in the DA54117. We go to the next slide.

And in the DL35041, summary of evidence, however, photo documentation is cited as occurring in each visit, typically, pre- and post-debridement. It is a primary source of evidence. And in one case, the photo documentation is cited as the only document used to verify the findings. On page 13, it talks about how there is a secondary examination to avoid bias. A clinician blinded by the treatment arm assessed the wound images for confirmation of healing condition. So this indicates that one of the primary evidence used supporting the necessity and the use case is photo documentation. So by not including photos in documentation requirements, the evidence that is relied upon by the physician is not presented as a supporting document as it is relied upon in the summary of evidence. So it's relied upon in the summary of evidence and other places and as a standard of practice, best practices, but it is not provided for in the documentation requirements. Next slide.

And as a expert in both cinematography and a little medical documentation, I also want to take a moment to raise some awareness around the lack of standards for photo documentation for wound care. I think all stakeholders could benefit greatly from improving this photo documentation. And I'll just give you a short summary. The next slide. So most often, we are photographing with the various different medical devices known as iPhones, and this is a typical iPhone. So if you've got a picture, this is a [inaudible]. I'm using a not real wound. This is a standard dressing wound, a fake wound that we have to represent this case. But it would seem to be true if you were taking this in different parts of the clinic. These are taken in different parts of the clinic, but the idea is rather than troubling a patient to go in different rooms at the same time, we simply use a model. But the standardization would enhance consistency, integrity, and reliability. So this is a picture taken with the same device at the same time in slightly different areas of the exam room, and it gives you an indication of how greatly the results can vary. We go to the next one. Did we skip a slide? There should be a slide-- there we go.

So using a consumer device with all of its designs primarily for social media and so forth, in a medical setting, we have potential for error that's really generated from the device itself, potentially presenting three different medical assessments. So this is the same wound on the same day, same visit. This is exactly the same wound model. This represents quite different approaches to medical assessment and the analysis that is derived from those photographs, which is commonly done in various different medical EMRs for wound care. They might also derive information that was incorrect or slightly off or erroneous. Go to the next slide.

So in conclusion, in summary, the wound documentation is part of the medical record, and it's relied upon to make medical decisions regarding skin substitutes. However, it's not provided for specifically in the documentation requirements. And I believe that physicians utilize photo documentation to assess and determine the medical necessity for skin substitutes in accordance with the coverage, guidance, and the documentation requirements. In fact, the vast majority of wound care EMRs, specific to EMRs, derive wound measurements as well as other data from the photo, making it a primary source of evidence. And this is strongly supported, as I said before, by the reliance on wound photos in the summary of evidence in the L35041, which-- the photos were used as the only documentation to verify the findings. That's on page 13.

Not providing for final documentation places both the clinician and, in this case, First Coast at a significant disadvantage by disregarding key portion of the medical record. This defies logic and appears contrary to the current requirements that state the submitted medical record must support the use of the selected ICD-10 code. In conclusion, the request is simply to specifically call out for the submission of photo documentation or allow for the submission of photo documentation in the requirements documentation so the physicians can present the full evidence that they utilize in the medical record and provide First Coast with a complete medical record. And lastly, I would welcome the opportunity to consider a future dialogue around how to improve the photo documentation in the field. Thank you so much. I don't know if anyone has any questions. I appreciate your time.

Dr. Juan Schaening

Thank you. Does any other of the other contractor medical directors have questions for the presenter? Then thank you again for your presentation. As I stated to the other presenters, you have until September 24th to provide any clinical evidence to support your request of how this photographic evidence could improve wound treatments on these patients receiving skin substitutes. So we appreciate your presentation.

Francis James

Thank you.

Dr. Juan Schaening

Let's move to the next presenter then. Our next presenter is Dr. Chris Pittman. No, excuse me. Our next presenter is Dan Leary, from Parametrics Medical. Please go ahead stating any conflicts of interest, Dr. Leary.

Christina Dohring

I'm Christina Dohring. I had to step in for Dan as he got called to a case today. Thank you so much for having me. My only conflict is that I am an employee of Parametrics Medical.

Dr. Juan Schaening

Okay. Thank you, Ms. Dohring. Please go ahead with your presentation.

Christina Dohring

All right. As a little background, Parametrics Medical was founded in 2008. We are FDA registered and AATD accredited, and we retain tissue banking licenses in all applicable states. We serve as the exclusive national provider of sports medicine tissue for DePuy Synthes Mitek. Next slide. We're here today to discuss two things: first will be our Restorigin amniotic membrane, with the request to move that to group two per our TRG opinion letter and the second to discuss the number of applications per patient. As a quick background, which I'm sure you all know, the regulatory requirements for an HCT/P are that tissues are minimally manipulated and intended for homologous use. Restorigin is processed in such a way that it does not alter the relevant biological characteristics of tissue, and it is intended to be used for the same basic function it performed in the donor. Next slide.

We do have our FDA TRG opinion letter. Per the TRG group, Restorigin, when intended for use as a barrier or cover for acute and chronic wounds, appears to meet the criteria for regulation solely under section 361 of the PHS Act and the regulations in 20-- pardon me, 21 CFR part 1271. Next slide. As a quick overview, Restorigin is a placental tissue allograft that may be used as a protective barrier in wound care applications. The natural properties of the amniotic tissues provide mechanical protection and act as a barrier to aid in the management of acute and chronic wounds. Next slide. Restorigin is a dual-layer amnion that provides for easy application due to its non-oriented configuration. It naturally adheres to the wound bed, and it's easily manipulated. The tissue is processed with gentle detergents and water rinses, and the grafts go through terminal sterilization via electron beam, which has been shown to be gentler on biologic components. Next slide. We'll go to the next. Thanks.

We have a case study specific to our membrane. As a quick overview of this study, there were 10 patients who had ulcer Wagner grades of 1 and 2. Five of the patients had type 1 or type 2 diabetes. One patient had peripheral vascular disease. All patients failed four weeks of standard care prior to treatment. The treatment protocol consisted of weekly or biweekly applications of Restorigin, and the median number of Restorigin applications was 3.5 and ranged from 1 to 7. As a result, 20% of patient wounds were completely healed after two weeks of initial application, and 80% of patients needed greater than two applications for recovery. But the great news is that on average, 94.6% of wound area reduction was observed after eight weeks of human amniotic membrane therapy. The study demonstrates that Restorigin therapy, graft therapy, is a safe and effective treatment for chronic non-healing ulcers. Next slide.

And then as part of this discussion, bringing it more to a personal level from a human perspective, we really did want to talk about the number of applications that are being proposed, that it be reduced from 10 applications to 2 applications, and how that would impact the patient population. This is a patient that you're seeing here, on this slide, who is facing amputation for severe venous insufficiency. The image is prior to the first application of Restorigin amniotic membrane, and all medical necessity requirements were met prior to this. This patient had gone through enormous amounts and was kind of at his last stage of hope for recovery. Next slide. This is the wound after the second application. The improvement is obvious, but under the draft coverage policy, this patient would have exhausted their coverage for treatment at this point. The likelihood that this patient would have digressed back to amputation is incredibly high. Next slide.

This is the wound after the seventh application, and today the patient is in full recovery and is living a normal life with both limbs. We see this story play out every day. There are hundreds of studies providing the efficacy of amniotic membranes, and all of them support between 4 and 10 applications. It is our opinion that reducing the number of applications to a limit of 2 will dramatically increase the number of non-healing wounds in the United States, and in fact, would increase the financial burden on the Medicare system. Final slide. In summary, Restorigin is a 361 with an opinion letter from the FDA. We'll be certain to submit all of our evidence and the TRG letter by the 24th. The case evidence supports the use of Restorigin in the treatment of non-healing diabetic wound ulcers, and there are hundreds of studies proving the same for amniotic membrane as a whole. Parametrics Medical respectfully requests that Restorigin Q4191 is considered for coverage in the group two, and we strongly request reconsideration of the maximum applications for treatment to remain at 10, as it is across national coverage currently. Thank you, everyone, for your time, and we appreciate being able to speak to you today.

Dr. Juan Schaening

Thank you for your presentation. We greatly appreciate it. Does any of the contractor medical directors have any questions for the presenters? Hearing none. I just want to thank her again and move forward to our next presenter. That is Dr. Chris Pittman from the Vein911 Clinic. Dr. Pittman, please go ahead, stating any conflicts of interest.

Dr. Chris Pittman

Thank you, Dr. Schaening. Can everyone hear me okay?

Dr. Juan Schaening

I can hear you well. Not that loud, but I can hear you well.

Dr. Chris Pittman

Okay. Perfect. I will try to talk louder. Yes. I'm Dr. Chris Pittman from Tampa, Florida [inaudible]. There are potential conflicts of interest [inaudible]. I am the CEO and medical director of Vein911 Treatment Center here in Tampa Bay area. I'm also a managing director of the largest [inaudible] practices in the country [inaudible] specialists. I'm a board member of the American Vein & Lymphatic Society. And I spent five years, from 2017 to 2022, as a [inaudible] for I am no longer [inaudible]. I appreciate everybody's attention. I came to speak to you also on behalf of the American Vein & Lymphatic Society, and I'd like to make a case for early [inaudible] [crosstalk]--

Mandy McGarvey

Dr. Pittman.

Dr. Chris Pittman

Yes.

Mandy McGarvey

Dr. Pittman, I apologize. This is Mandy, the host. We are having a lot of difficulties hearing you. Are you able to connect via phone rather than a computer?

Dr. Chris Pittman

I apologize, Dr. [inaudible].

Mandy McGarvey

Your audio is very poor, and we can hardly understand anything that you are saying.

Dr. Chris Pittman

I'm really sorry. Yes. Let me [inaudible] [crosstalk]--

Dr. Juan Schaening

Dr. Pittman, this is Dr. Schaening. Let's do something. Try to connect by phone. Mandy, can you help him so he can connect by phone? And then we can move to the next presenter and allow Dr. Pittman the opportunity to speak when he has a good connection.

Mandy McGarvey

Perfect. Yes, thank you.

Dr. Juan Schaening

Okay. Work with Dr. Pittman, and let's move to the next presenter. Thank you. Give me a second here. I hope the next presenter is ready [laughter]. We appreciate you giving us the opportunity to help us with the time management here. So our next presenter is Jeffrey Shapiro with Hyman, Phelps & McNamara. Please go ahead, stating any conflicts of interest.

Jeffrey Shapiro

Okay. Can you hear me?

Dr. Juan Schaening

Loud and clear. Loud and clear.

Jeffrey Shapiro

Excellent. Okay. I am ready to jump ahead and help you with the time management. I don't really have any conflicts. The only thing I put down is that I do-- somebody's got music playing. I do provide legal counsel to a number of-- and have provided legal counsel to a number of firms in this space in the last 24 months. I don't think it's a conflict, but it is on the form. Shall I proceed?

Dr. Juan Schaening

Yes. Please proceed with your presentation. Thank you.

Jeffrey Shapiro

Okay. Thanks. So I have a Word document with speaking points rather than a PowerPoint, but if you could roll ahead, Mandy, to whatever the next slide is, if it came in as a slide. Or do you not have it, or you're not showing it, and I should just speak to it?

Mandy McGarvey

I didn't receive a-- I didn't receive a PowerPoint. I just received speaking points.

Jeffrey Shapiro

Right. I thought that was your preferred format. Okay. So you're not going to show that?

Mandy McGarvey

Right. There won't be a PowerPoint slide. It'll just be a slide with your name.

Jeffrey Shapiro

Okay. Okay. Very good. So, my name is Jeff Shapiro. I'm a director at Hyman, Phelps & McNamara, which is a DC-based law firm specializing in FDA regulatory matters. The firm was established 40 years ago. I've been practicing with the firm for many years, and I have about at least two decades experience with FDA's regulation of 361 HCT/Ps. I was actually around during the creation of that process, and I've practiced in that area ever since. So as long as FDA's been doing it, I've been doing it. And that's my experience base. And I'm speaking today here on behalf of the MiMedx Group. And the topic is a concern that the First Coast Service Options and Novitas Solutions, Inc LCD has not given 361 HCT/Ps skin substitute manufacturers sufficient time to obtain a TRG or Tissue Reference Group letter.

Jeffrey Shapiro

This FDA group can get backlogged and does not have a guaranteed time frame for requests, and it is therefore a concern about the timeliness of being able to get these letters. So let me just level-set everyone by just beginning by mentioning a little bit about what the TRG is. The Tissue Reference Group, or TRG, is FDA's single cross-center reference point which reviews and makes legally non-binding recommendations concerning the classification of HCT/Ps as 361s are not. The composition, they've got three members from the Biologic Center, CBER, including a product jurisdiction officer, three members from the Device Center, including a product jurisdiction officer, a liaison from the Biologic Center's Office of Compliance and Biologics Quality, OCBQ, which oversees much of the tissue program. They also have a liaison from the Device Center's Office of Product Evaluation Quality, or OPEQ, and a representative of the Office of Chief Counsel, which is the FDA's internal legal counsel, and a liaison from the Office of Combination Products, which also plays a role in these decisions or as to a 361-- whether a tissue meets the 361 status or not.

So that's the lay of the land as far as what the TRG is. Now, what is a TRG letter? Normally, manufacturers of HCT/Ps, which are human cellular and tissue-based products, self-determine. Legally, they're entitled to self-determine whether their products meet the requirements for 361 status. And if they do, then the product is listed with FDA, but there's not a pre-market review. If the requirements are not met, then the HCT/P is still regulated under the HCT/P regulations, which are 21 CFR part 1271, but they're also subject to regulation as a biologic, a drug, or a medical device, which may require some sort of pre-market review. So more than 20 years ago, FDA established a voluntary program in which a manufacturer of an HCT/P could submit a written request to the TRG to advise whether their product was a 361.

Many manufacturers actually do not have occasion to use that voluntary program. And so the LCD, in this case, for this class of products is effectively converting it to a mandatory process, at least for getting reimbursement. And that will be an additional burden on industry and on FDA, specifically the TRG because it will increase their workload. And some manufacturers may have multiple products. Typically, they're submitted as separate products to the TRG. So in other words, it's not by manufacturer; it's by product and potentially product family. So in the process, the manufacturer submits a request that fully describes the product to the TRG and usually has some analysis as to why the manufacturer believes the product meets 361 requirements. And the TRG reviews these on a first-come, first-served basis. They only convene twice a month to make decisions or recommendations. So once a new request moves to the top of the queue, however long, the TRG will review it and provide a letter with some non-binding advice on the product's classification based on the information provided to the TRG.

The recent LCD requiring TRG letters for skin substitute has a deadline that is too short, just to speak frankly. It apparently became clear that this requirement would be promulgated on August 11th, when the LCD was issued. An earlier draft, basically, it appeared to grandfather the products that already have coverage. The August 11th version appears not to have that grandfathering provision or nature, and so even those in industry who promptly filed TRG requests-- in fact, those that have filed it already this month are likely to miss that deadline because the comment deadline is September 24th. The TRG targets a 60-day response time. That's according to their written internal SOP, which is available on their website.

So if you submit on August 15th-- if you submit it on August 15th, mid-October is your target for the TRG to issue a advice or determination, which would be after the September 24th LCD comment deadline. And that 60-day figure is actually a rosy scenario because I can say that in 20 years of practice, the TRG does not always hit that 60-day target, and it may miss it by many months. It really depends on their workload, which is not predictable. The fact that they only meet twice-- it's the first and third Monday of every month. And also, this LCD may itself spike their workload if enough companies have to submit additional requests. So it's predictable that many companies requesting TRG letters will not receive them before the LCD comment deadline of September 24th. And as a result, patients may lose access to well-studied provider-preferred products.

I want to contrast that, the approach taken in this draft LCD, with the approach taken by CMS, which is allowing much more time to transition to a TRG letter requirement. So in the CMS PFS proposal, if it's finalized, the deadline is currently the end of 2023 to obtain a TRG letter confirming 361 HCT/P classification. So that's in contrast to September 24th of this year. These transitions, in general, is-- this is not the first time this has happened. And I will say from observation that these transitions to some sort of TRG letter requirement are not easy, and I would urge the organization to allow ample time. And just as a short reminder, consider the history of the Defense Health Administration, DHA, action on this topic.

In early 2020, without much notice, DHA began requiring written confirmation from FDA of 361 HCT/P status. And frankly, the TRG letter was the easiest and most direct way to do this, so it was effectively a TRG letter requirement. In the end, the policy actually proved unworkable. Some manufacturers stopped doing business with the DHA, veterans lost access, and ultimately, earlier this year, the requirement was rescinded. Now, this kind of lost access and rescission of the policy in the end may not happen here, but implementing the new policy too abruptly is bound to cause dislocations that may cast doubt on the wisdom of the draft LCD. So this is not a challenge to the new policy; if it's believed that this requirement is necessary, that's fine. I'm merely suggesting that a deadline extension is in order and will help smooth the transition to the new policy and better assure the ultimate success of the policy.

And there are two potential ways that this could be done. One, you could simply adopt the same timeline as the CMS proposed PFS rule, which is the end of 2023. Or if that's too, for whatever reason, far out, I would recommend defining a transition period of not less than 6 months and preferably 12 months. And that will allow manufacturers to spread themselves out or at least if the TRG has a spike, allow them to work through the backlog. And it will allow sufficient time for everyone to get their ducks in a row, especially products that are already on the market where there's a concern about a gap in coverage. So that concludes my remarks, and I want to thank you for this opportunity to share these views. I'd be happy to take questions.

Juan Schaening: 02:16:35 Thank you for your presentation. We greatly appreciate it. Does any of the contractor medical directors have any comments for the presenter or questions? So, we will appreciate if your requests and comments are sent in writing and supported by published documentation. In addition, I want to point out that you're quoting correctly the 2023 Physician Fee Schedule proposal, but I want to point out that in the 2022 Physician Fee Schedule rule, there's a statement from CMS in the final rule that was approved that is in place for the year 2022 that says that, "Manufacturers of HCT/Ps should consult with the FDA Tissue Reference Group or obtain a determination to a request for designation on whether their HCT/Ps are appropriately regulated solely on the 361 update [inaudible] and the regulations in 21 CFR part 1271." So, we acknowledge your request. Please send it in writing. We will address it as part of our comment response document.

Jeffrey Shapiro

Okay. And can I make just a brief comment to your comment? Which is, yes, there's been advice, and frankly, manufacturers always have this program available to them. There are all kinds of reasons why they might consult with a TRG. But they don't have to do it, and many times, they won't do it unless they have to do it, and if they have to do it, they will. And so when you switch to a rule where they have to do it, it will just be-- it will go much more smoothly if you allow them sufficient time from that point rather than saying, "Well, you should've done it earlier." And I think in this case, people may lose access unnecessarily and inappropriately if there's not a transition period of sufficient length starting from now.

Dr. Juan Schaening

Thank you. So, let's move forward. We appreciate your presentations and your comments. So our next presenter I believe is Dr. Chris Pittman that is ready right now with good audio. And he's going to present from Vein911 Clinic. He has already made his conflict-of-interest statement, so he can go forward to his presentation. Dr. Pittman, please present.

Dr. Chris Pittman

Mixed up. I'm on so many different platforms that it co-ops the microphone. You can hear me okay?

Dr. Juan Schaening

Now I can hear you okay. Mandy, do you agree? For recording purposes, is it good enough?

Mandy McGarvey

Yep. I mean, the little bit that I heard, that sounds a lot better than what it did.

Dr. Juan Schaening

Okay. Let's move forward then, Dr. Pittman.

Dr. Chris Pittman

Okay. I am speaking on behalf of myself and the American Vein & Lymphatic Society. And I'd like to make the case for early and accurate superficial venous insufficiency diagnosis and treatment in chronic leg ulcer patients before employing skin substitutes. And I will simply state our recommendation and then back it up with some comments. Fortunately, my presentation is short and is backed up with a bibliography previously submitted to First Coast. We recommend a requirement that all chronic leg ulcer patients be referred for a high-quality ultrasound exam to detect superficial venous insufficiency and that diagnosed superficial venous insufficiency be appropriately treated before the use of skin substitutes.

The overwhelming majority of chronic leg ulcers are due to venous disease, not arterial disease. The sheer prevalence of superficial venous insufficiency is why most chronic leg ulcers originate from venous disease and not arterial disease, yet payers typically have no requirements or cursory requirements for the evaluation of venous disease in chronic leg ulcer sufferers who present to wound care centers for treatment. Nearly 80% of chronic leg ulcers are caused by undiagnosed and untreated vein disease. Thus, the overwhelming majority of chronic leg ulcers are more accurately described as venous leg ulcers. SVI, or superficial venous insufficiency, is hereditary, and 60 to 80 percent of Americans will suffer SVI in their lifetimes. Nearly 10% of 20-year-olds, by the time a teenager turns 20 years old, male and female will have demonstrable superficial venous insufficiency on ultrasound exam.

Personal communication with experienced wound care physicians who also understand the significance of SVI in chronic leg ulcer patients report that, one, 90% of chronic leg ulcer patients they treat have underlying venous disease; two, evaluation for SVI and treatment of SVI should be standard of care; three, they ultimately use skin substitutes in a small minority, less than 10%, of chronic leg ulcers that they eventually heal. Too many VLU or venous leg ulcer patients are treated by wound care centers that manage the ulcer instead of directing care to the underlying venous insufficiency that caused the ulcer, leading to high recurrence rates and ulcers that never heal or heal only temporarily, costing billions every year.

The average annual incidence of VLUs in Medicare beneficiaries is 2.2%. VLU patients use more medical resources and incur annual incremental medical costs of $6,391 in Medicare and $7,030 in private insurance. The estimated annual US payer burden for VLUs is $14.9 billion. To put this in perspective, the estimated burden on public and private payers for diabetic foot ulcers only ranges from 9 to 13 billion. This is because SVI is much more common than diabetes.

In our great state of Florida, the estimated annual burden of VLUs on Medicare and private insurance is $1 billion. When chronic leg ulcer patients are referred to a qualified vein care specialist, the vein problem causing the ulcer in the first place can be properly diagnosed and treated cost effectively. In a 2018 landmark New England Journal of Medicine article that was randomized controlled perspective was published, concluding that, I quote, "Early endovenous ablation of superficial venous reflux resulted in faster healing of venous leg ulcers and more time free from ulcers than deferred endovenous ablation. Anecdotally, vein care experts have seen no appreciable change in VLU patient volume in the intervening four years. The majority of patients receiving wound care in the USA today are undertreated because they never receive appropriate SVI diagnosis, and consequently, they--" excuse me. I have an incoming phone call, but I'm not going to answer here. "Consequently, they never receive appropriate treatment of their underlying SVI that is causing the VLU in the first place."

The landmark 2018 New England Journal of Medicine article proved that low-cost venous treatments heal VLUs using the ablative techniques of thermal ablation, both radio frequency and laser, and ultrasound-guided foam sclerotherapy. Ultrasound-guided foam sclerotherapy is an effective, low-cost method to eliminate problem veins at their source using ultrasound to inject a chemical agent through a needle. The vast majority of VLU patients also never received ultrasound-guided foam sclerotherapy, so their wounds rarely heal durably, funneling millions of dollars to wound care centers.

In summary, it is clear that appropriate venous care cannot be delivered if chronic leg ulcer patients are not appropriately and accurately diagnosed in the first place. Thus, we recommend a requirement that all chronic leg ulcer patients be referred to a high-quality-- be referred for a high-quality ultrasound exam to detect superficial venous insufficiency and that diagnosed SVI be appropriately treated before the use of skin substitutes. In conclusion, ultrasound exam of the superficial venous system is a surrogate for the presence of SVI. However, ultrasound is notoriously user-dependent imaging modality. Therefore, only qualified experienced vascular technologists with SVI experience should perform an SVI exam.

Recognized ultrasound technologist credentials include the RVT and the RVS. However, Medicare should also recognize and include the RPhS designation known as a Registered Phlebology Sonographer Credential. Those who hold the RPhS credential have specialized training and experience with venous vascular disease. While the RVT and RVS credentials are rigorous, RVT or RVS typically have very limited experience with the diagnosis of lower extremity superficial venous insufficiency. Thank you for your attention.

Dr. Juan Schaening

Thank you, Dr. Pittman, for your presentation. It's greatly appreciated, as well as your enduring commitment to the health of our beneficiaries is duly noted. So any of the other medical directors have any question for Dr. Pittman? Hearing none. I just want to thank him again for his presentation, and let's move forward to the next presenter. Our next presenter is Marshall Medley from BioLab Sciences. Please go ahead, stating any conflicts of interest.

Dr. Marshall Medley

Good afternoon, everyone. I am the new chief medical officer of BioLab. That's my conflict of interest, as well as some stock options associated with that employment. I will be submitting these comments within the 45-day window you have mentioned a few times. I am somewhat new to this arena, being a brand new chief medical officer, but not new to practicing medicine. I'm here on behalf of my employer, BioLab Sciences, an Arizona-based company where I serve as their CMO. I'm here to discuss the proposed changes in the LCD for HCT/P, specifically our products with the Q-codes of 4205 and 4226. I would like to say I echo what many others have said in caring for these wounds thus far in this meeting. I recently retired from practicing medicine for more than 25 years. That was about three weeks ago. During my career, I was the director of two separate wound care centers, and I practiced as a board-certified vascular surgeon. I've seen my share of wounds and, of course, done my share of amputations due to these wounds. I'm here to discuss some of the proposal changes noted in your recent LCD and what ramifications they might have on physicians trying to take care of patients. I will take a little bit different approach, as others have obviously explained the science.

In 2019, a revision was made placing our products Q4226 and 4205 in group two. My comments will include the quotes from those letters. This new LCD has shown that our Q-codes have been changed along with many others apparently to group three. I say apparently because I cannot find anywhere the current group two and group three members. Since there is no reason listed for the proposed changes and we've not heard those, I can only make assumptions behind why these were changed. So assumption number one, perhaps you do not accept the data from other manufacturers to support our product. In order to answer that assumption, I'd like to use an analogy. As a vascular surgeon, we used to perform and many still do perform carotid endarterectomy very frequently on patients with carotid stenosis. This was done to prevent stroke.

The data behind the prevention of stroke doing this procedure as well as stenting of carotid arteries is very well known. I was involved in the training of general surgeons and vascular surgeons, and we taught these residents and fellows how to perform this procedure. Once they learned how to perform the procedure and they were tested on it and became board certified to do the procedure, they were allowed to do the procedure. They did not need to collect data on their own patients. They did not need to show data that they were doing well. They simply needed to be board certified and continue with CME. The data that they had on carotid endarterectomy was there. They needed to know the data. We just needed to make sure they were qualified.

In like manner, the data for these products is there. Many articles have shown the safety and efficacy of these products. Many manufacturers have provided this. Having every single manufacturer produce the same data is counterproductive and unnecessary. One just needs to make sure that the product being produced is in compliance with the standards set by the FDA. Those standards for a 361 product include minimal manipulation, intended for homologous use only, that it's not combined with any other article, and that it does not have a systemic effect and is not dependent on the metabolic activity of living cells. Since we meet all these criteria and we have data from other sources supporting the safety and efficacy of these products, then I respectfully argue that any lack of data from our manufacturers should not be a reason to move our product from group two to group three. In the same manner, we are in good standing with the FDA and following its guidelines and regulatory requirements. Based on the current guidelines, BioLab Sciences products Membrane Wrap and Dermistat are HCT/Ps and registered as such with the FDA without further requirements to be sold or distributed in the market. According to the draft article, HCPCS codes will be considered for coverage if meeting the FDA regulatory requirements and criteria, which ours do. We also have the FDA letter that was mentioned in another presentation today, and we will send that with our comments.

Assumption number two, perhaps the MAC region decision-makers are not satisfied or do not agree with the myriad of articles showing the safety and efficacy of these types of products. My answer, there are many articles regarding the efficacy of these products. They show the safety and efficacy on these wounds. The goal of any of these products is to cover and protect the wound, as well as to stimulate it from a stalled state to allow it to heal quickly and prevent sequela and subsequent worsening in the patient's health. After practicing for 20 years, I can give you dozens of anecdotal instances where these products stimulated a wound to heal which was previously not progressing. One only need to spend some time in a wound care center to see the tremendous benefit.

Assumption number three, perhaps you do think that these products help the wound or prevent further issues. Answer, I have done my fair share of leg amputations. Despite numerous different treatments, some people do not heal. The detrimental effects of amputation is well documented, and the cost is extraordinary. How many amputations need to be prevented before the benefits of any wound care product to be noticed? Is it a financial issue? If it is, I assure you that it is less expensive to care for a wound with any products needed than to care for an amputee. Even if the amputee is functional, the prosthetics are expensive. I have not even mentioned lost time at work and multiple other social and economic issues suffered by the patient. If I can get someone back to work sooner with these products, then everyone wins.

Assumption number four, perhaps you do not want to pay for these products anymore. Answer, bean counting is something we all need to do. I get that. I would like to give you the bean counting I have seen in my years of practice. We see patients week after week and month after month with nothing to offer them except conservative care, including debridements and office visits. These numbers add up, and it adds up for the patients too because they have to use their copay, and some of them have the 20% that they have to pay on top of the Medicare coverage. The lost time at work causes a burden difficult to bear. So how many wounds do we need to heal before we make a dent in the finances? What wounds need expensive products, and which do not? Sadly, the discussions tend to move toward finances and not patient need. Let's just focus on the patient for right now. The patient wants to be healed as quickly as possible. The doctor wants to do what he or she can to help them heal quickly because they know what can happen the longer the wound is open. Perhaps all you want to do is be more prudent with your money. That is completely understandable, but it must be done in a way that is not detrimental to the patient health. And I feel relegating these products to a group that will not ensure payment is doing just that. Moreover, there is cost related to the additional patient visits than an open wound demands, which would increase the overall cost of treatment. This is something overlooked when evaluating inherent benefits of a product.

Now, I'd like to emphasize this: your proposal states a lot of criteria for HCT/Ps to be used. A lot of them I happen to agree with. I feel the patient should have vascular studies, vein and arterial studies done, and have their nutrition and diabetes optimized, that they need good off-loading and compression. I think all of the standards of care should be documented and done on all of these patients before these products are used. I will admit some people use them before the standard of care is over. These products are not first-line, and conservative therapy should be utilized first. In emphasizing these things, you help the providers understand that things should be happening with the wound before these products are used, which is good common-sense medicine.

But please understand the unintended effect of placing these products in group three. You're essentially taking them out of the toolbox, not allowing us to use them when we need to. Instead, allow us to use them prudently. Have us show of what we have done and why we want to move these-- why we want to use these products. Take them away in a-- taking them away is a decision that will have tremendous negative ramifications to all involved, including CMS and the MACs. You will pay more for these wounds and for a longer time. These products are becoming the standard of care, and my practice will use off all the usuals mentioned above and have the wound stall for several weeks before we start using this. When infection and other issues have been addressed, we are looking at a wound that is clinically stalled and needs a jump start, and these products help with that. They provide growth factors and a scaffolding that will help the wound get into a proliferative phase. Do not take this away. Instead, provide a way for us to use them prudently. I appreciate the finances, but there should be a middle ground.

In conclusion, the use of these products has become nearly the standard of care. To cease reimbursing these products and therefore keeping them from thousands of patients' wounds would be significantly detrimental. These products accelerate wound healing and help move stalled wounds to the proliferative phase. Taking away these products through eliminating reimbursement will delay healing and essentially increase cost by prolonging the number of clinic visits, debridements, comorbidities such as infection, and of course, dramatically increase costs due to hospitalizations and amputations. I've had to make assumptions here because we cannot find the reasons behind your proposal. Hopefully, I've hit on a few of them. Not reimbursing these products will essentially eliminate them. Likely no manufacturer will be able to produce them with little to no reimbursement. Our ask is for you to rethink the proposal and put these products, including ours, back into group two. Many of us will gladly help set up protocols for use, which makes sense for all involved, making the patient the main priority, followed by finances. Do not hold the patient and their wound hostage; allow us to care for them the best way we know how and with the best tools possible. We all need to be responsible with how these products are used. We are more than happy to be a part of the solution and not a part of the problem. Thank you for allowing me to speak today.

Dr. Juan Schaening

Thank you. We greatly appreciate your presentation. I get the comment. It's the intent of this contractor to provide access and coverage to a skin substitute graft proven to provide scaffolding and healing of wounds, as well of human cell tissue products that provide scaffolding and healing of wounds that have proven clinical evidence and that are in compliance, have evidence of regulatory compliance. And that's why we're emphasizing on this comment period to manufacturers to provide us the letter supporting the regulatory compliance and any additional evidence that they can support of these agents or these products [inaudible] wound treatments in healing these wounds by providing a scaffolding and healing. So just wanted to emphasize that I have really no comments. I really appreciate your well-thought presentation.

Dr. Marshall Medley

I appreciate that, and we will get all of those documents together within the 45 days and get you what you need.

Dr. Juan Schaening

Thank you. So let's move forward then to our next presenter. Our next presenter is Dr. Eric Lullove with West Boca Center for Wound Healing. Please go ahead, stating any conflicts of interest, Dr. Lullove.

Dr. Eric Lullove

Thank you, Dr. Schaening. Can everybody hear me okay?

Dr. Juan Schaening

Loud and clear.

Dr. Eric Lullove

Great. My conflicts are I am currently representing the Wound Healing Society from a society standpoint. I'm representing myself as a stakeholder and a practitioner within the state of Florida as the chief medical officer for the West Boca Center for Wound Healing. My other conflicts of interest, I am a clinical scientific investigator for Kerecis as well as for BioStem Technologies. I previously addressed this committee and this hearing back in May, so I am not going to make any additional comments based on what I had already submitted and what I had already discussed. I, however, am going to comment on the changes that were made in the current policy that still are, to my dismay-- the thought process with the contractor is still beyond comprehension. I do not understand the current thought process behind the contractor - and I'm talking about Guidewell in general, both the parent company of Novitas and First Coast - on where these decisions are coming from.

My first comment is going to be based on the billing and coding article, where even though you're allowing companies-- and this goes for the entire industry as a whole, every manufacturer, with respect to the contractors. And you have stated, "It is recommended that the manufacturer of the particular skin substitute or CTP obtain the appropriate information for FDA regulatory compliance and send it to the MAC." Now, that all sounds well and good, verbatim-wise. However, you as a contractor have not given a specific pathway on time frame and when the product will be considered for coverage and placed into the appropriate code group. Who is making the consideration on that part? Are they an expert in HCT 361s? Do they have experience with 510(k) products?

There is not enough information in this billing and coding article to make me feel comfortable that the contractor is going to be jurisprudent in its decision-making as to which manufacturers who submit the proper paperwork with TRG letters-- when and how they're going to get placed into group two. So that's my first comment. And to not allow and to not have a transparent process is, to me, a gross negligence on behalf of the contractor. That's completely gross negligent because they're doing legitimate work to give you the paperwork and the documentation, and you have a fiduciary responsibility to the providers that are providing these services to make sure that those products are timely placed into the policy. So that's the first one.

My second comment is more of a clinical base. And I want to reference Dr. David Armstrong, who is one of the more renowned reference physicians in the space for diabetic foot ulcer healing. Dr. Armstrong has over 60,000 citations. He is a leading expert in diabetic foot ulcer treatment out of University of Southern California, and his study that was published in 2021 in July in the Journal of Wound Care was a North American supplement, Volume 30, Issue Number 7, and it was using CMS data on a total of 948,000 patients with a eligible lower extremity diabetic ulcer group of about 54,642 patients, and those patients who received advanced therapy versus non-advanced therapy.

Now, when we break this down, and his study completely broke it down by state, where if we look at Florida perspectively, there were 3,846 total episodes in the years that were studied. And there were 2,415 advanced therapy care versus 1,431. That put Florida in group eight in his study block, which had a reference range of 62.79% advanced therapy and 37.21 non-advanced therapy. As a result of those numbers and extrapolating the data from that compilation of Medicare data from ED visits and amputations and readmissions, okay, in reality, that three years of Medicare-approved treatment outcomes for patients with lower extremity diabetic ulcers had statistically significant reductions in rates of major and minor amputations, emergency room visits and hospital readmissions when advanced therapy was used in accordance with existing foot ulcers versus non-advanced therapies.

This coverage policy in the reduction of advanced therapies is going to increase the cost to the system. It is going to increase the rate of both minor and major amputation. It is going to go completely against CMS's Hospital Without Walls initiative that they released in 2020. It is going against the move to outpatient therapy, which CMS approved in 2015, 2016. And everybody seems to forget that the reason why you're seeing an uptick in applications of these tissues was because of an epidemic pandemic that we had for the last two and a half years, that wound centers were closing. Hospitals closed their wound centers, so you naturally saw an increase in data for physician office-based therapies and ASC therapies because of the move away from hospital wound centers.

So all I'm asking is that the data that you are looking at is responsible, because it's your data. The data was released as-- it was available from CMS. You are looking at the same data that I'm referencing in this study, okay? And the reality of all of this is that it's your own data that you're going against. This policy goes against your own data that you have in these episodes that I'm referencing out of this study group. And when you look within this study - and I'm going to put the study in my comments that will be submitted by September 24th - in the states that had lower advanced therapy applications, they had higher rates of amputation. Plain and simple.

One of the other things I would like to discuss is the cost of amputation relative to the lack of advanced therapy. So the way this works is that when patients who have a diabetic foot ulcer and wind up with a major amputation-- what winds up happening is there's a cost of care on the backside of this that everybody tends to forget about, okay, and that economically, the annual burden for diabetic foot ulcers ranges anywhere from 9.1 to 13 billion, okay, but in large part of increased hospitalizations, home healthcare, emergency room visits, and outpatient physician office visits. The reduction of major amputations has a long-term effect on ongoing health costs, and we are all in the business in wound healing about reducing amputation. Your policy that you have as a draft is going to increase that. I will guarantee it, okay?

In 2010, the estimated number dollar spent per patient post-amputation was roughly $60,000 with care costs in subsequent years of about 44,000. It is significantly cheaper-- I'm going to repeat this so that everybody at First Coast and Novitas can hear me clearly. It will be significantly cheaper to maintain advanced therapy protocols for tissue products for these patient populations than it will be to cut off their leg or part of their foot. You are doing your own beneficiaries a disservice by reducing this policy. You are making my job harder, and that's not the plan.

On top of it, once these patients have an amputation, they have a correlated five-year mortality rate, an increase in their mortality rate. So in essence, one can draw a conclusion that this policy, relative to this study, which is CMS's own data and First Coast's data, will lead to an increase in five-year mortalities of the patients that you are sworn to protect under the Social Security Act. I'm going to let that sink in for a second. Because it won't be my fault. It's going to be your fault. And those of you sitting in Jacksonville and in Dallas who think that this is a good policy, I want you to think about your grandparents. I want you to think about your parents and your friends' parents who need these services who are not going to be able to get them. That's what this comes down to. It's do you want your family members subject to this policy? Because that's what you're doing.

And in conclusion, I just-- in conclusion, I don't have much more to say about this. I'm just very upset that the contractor continues to write policies without coming to those of us who are expert stakeholders to help you write a policy that makes sense. This doesn't make any sense. It doesn't. It's cruel, it's inflammatory, and it's extremely disheartening. I've been doing this for 20 years, and I don't think I've ever seen a draft article that's so blatantly prejudicial to a specific subset of patients and punishing them for a genetic disease that they may or may not have developed as they grow into adulthood. And you have a fiduciary responsibility to protect these patients. I understand that you have a fiduciary responsibility to protect the trust fund, but not at the expense of losing patients' lives. That's where I got to draw the line, and this is where you guys are wrong. And that's why this policy needs to be dumped.

You cannot go forward with this policy on the basis of the fact that you're looking at it from a fiduciary standpoint. The data's there. The data's been there for 20 years. And when it comes to all of these other 361 products and products that are 510(k) approved and ones that go through a 351 pathway or a PMA 388, it doesn't matter. I'm inclined to agree with my previous colleagues that have testified to this committee and to these medical directors. We know it works. We'll get you whatever data you require, but not at the expense of losing-- not at the expense of losing patient limbs and potentially their lives. It's not worth it. With that, I yield back. Thank you very much for your time.

Dr. Juan Schaening

Thank you for your presentation, Dr. Lullove. Any comments or questions from the other contractor medical directors? Thank you. I just want to make a comment that cost is not really a driver on the decisions of a Medicare contractor. We made the decisions based on the available evidence, trying to identify what we would consider reasonable and necessary based on the evidence. Cost, between products costs, is not one of the elements that we evaluate when we develop a local coverage determination. We will cover any reasonable and necessary product that is safe and effective, [as effective, as available?] or available alternative that is available and proven through the evidence. But we greatly appreciate your comments. Let's move forward to the next presenter. I--

Dr. Eric Lullove

Dr. Schaening, I appreciate your comments, but I'm going to disagree with you because I've been doing this for 20 years in this jurisdiction. And trust me, cost is always-- it may not be the primary, but it's certainly in the conversation. And I'll let you move on. Thank you.

Dr. Juan Schaening

Thank you. And have a good day and I appreciate that comment. So let's move forward to the next presenter, Marcia Nusgart from the Alliance of Wound Care Stakeholders. Please go ahead and state any conflicts of interest and present.

Marcia Nusgart

Thank you so much. It's been a long afternoon. I feel that we should have a stretch break or something like that. But that should've come probably a few minutes before that. My conflict of interest is the fact that I'm the CEO of the Alliance of Wound Care Stakeholders, and our members do pay a membership fee to be a member of the Alliance. We appreciate the opportunity to provide the Alliance's comments on the draft skin substitute LCD and accompanying LCA. And the Alliance is a non-profit multidisciplinary trade association of physician medical specialty societies, clinical and patient associations whose mission is to promote quality care and access to products and services for people with wounds through affective advocacy and educational outreach in the regulatory, legislative, and public arenas. So these comments were written with the advice of our clinical specialty societies and organizations that not only possess expert knowledge in complex chronic wounds but also wound care research. You can find a list of our members on our website.

The Alliance does still continue to be concerned with this draft policy. We identified many issues and recommendations not only in our public comments that I gave on April 28th, but also in our May 27th, 2022 comment letter. We took writing our comments very seriously and spent considerable time on them due to the negative impact that these LCDs and LCAs make in our members and the patients that they treat. Our comment letter was very unique in that we hoped to make it easy on those that were reading it to frame our concerns and recommendations in a chart to make them easier to understand. And we also provided a redline copy of the LCD and LCA and identified our recommendations in red.

So I'm stumped. It was kind of unclear to us why First Coast reissued the same draft policy while not taking into consideration any of our comments offered. If First Coast was really interested in further comments, then it would've been wonderful to release a draft policy taking into consideration our already provided comments, which would've been a more useful exercise rather than a very narrow scope, which is what you had done. So we still stand behind our comments, the oral and written ones. I'm not going to reiterate it because that's what you asked us not to do. But in terms of the limited changes that you did address in this new draft policy, let me be clear. The Alliance does not support the movement of any products into the group three, non-covered list during an active comment period, nor does the Alliance support the placement of products into the non-covered list when the MAC has not and continue to not be transparent in the evidentiary requirements.

If the MAC is moving products into the non-covered category, one needs to be able to clearly identify the reason for this movement. And if the MAC simply just has not received a TRG letter from the manufacturer, we don't believe that's a good enough reason to move the product, as the TRG letters take much time to receive. We understand that even CMS will be allowing companies up to 2024 to obtain these letters. And I believe that Jeff Shapiro earlier had stated this very eloquently, how long it takes for a manufacturer to get a TRG letter in this area and the disconnect between what First Coast has done for deadlines versus CMS.

Furthermore, as a procedural issue, this is a proposed policy. It has not been finalized. As such, the requirement obtaining a TRG letter should not be the determining factor as to whether a product is in the covered versus the non-covered list. Once the policy becomes finalized and the requirement is final, then the MAC should provide a date by which these TRG letters are required to be provided in order to stay in the covered grouping. If there are other reasons the MAC can move products in this active comment period to the non-covered list, the MAC is required to identify the rationale for moving these products. It's not clear and it's disruptive to patient care.

Finally, we wanted to compliment you and the fact that First Coast had used the term cellular and/or tissue-based products for skins wounds or CTPs along with the term skin substitutes in your draft policy. But we'd love for you to take into consideration to totally eliminate the term skin substitutes. We have stated both in previous oral as well as written comments the problems with using this particular term. So we would respectfully ask you to not use the term anymore in your final policy. And even in the title of the policy, it should be CTPs or cellular and/or tissue-based products for skin wounds instead of skin substitutes.

As such, we are happy to serve as a resource for First Coast medical directors. And as Dr. Lullove mentioned, you have a whole group of medical experts that can help you in terms of working with you and serving, as the Alliance does, as an unbiased multi-disciplinary knowledgeable clinical resource for information as a collaborator and can address any wound care-related subject matters. Our members consist of physicians and surgeons, podiatrists, physical therapists, nurses, dietitians, and we can help you with technical questions, creating educational seminars for the staff, convening educational seminars and CTPs, which we had a fabulous one with CMS staff just a few months ago. So we hope you'll utilize our expertise to help to ensure that this policy is well balanced and clinically accurate. Thank you very much for your time.

Dr. Juan Schaening

Thank you. I appreciate your presentation. Does anyone of the medical directors have any questions for the presenter? Thank you. Then I'm just going to make a comment. We appreciate your presentation. The intent of this contractor, as stated multiple times during today's meeting, is to provide coverage to agents that are wound treatments that are skin substitute graft or human cell tissue products. And the reason that we still use that term-- and we will acknowledge that in our comment period, but when we've wrote the original draft is that, remember, we are paying per coding. When there's a reasonable and necessary surgical skin substitute graft application, we will pay the skin substitute graft or human cell tissue product or the product that can be billed with that surgical skin substitute graft application code.

So, the CPTs still use that terminology in the payment of these products when billed in conjunction with a reasonable and necessary surgical application of a skin substitute graft. But all comments that were received on the previous 45-day notice comment period are going to be addressed. The intent of this LCD was to provide additional time for manufacturers to provide us the regulatory information as well as any clinical published evidence that would support the use of these products as wound treatments. But all comments that were received on the previous comment period are going to be addressed on our response to comment document. So I greatly appreciate your comments, and I just wanted to reassure you of that. So let's--

Marcia Nusgart

Thank you very much. I expected that.

Dr. Juan Schaening

Okay. Sure. So let's move to our next presenter. Our next presenter is Karen Ravitz from the Coalition of Wound Care Manufacturers. Please, Ms. Ravitz, go ahead and express any conflicts of interest.

Karen Ravitz

Great. Thank you, Dr. Schaening. I hope you can hear me okay. Can you hear me all right?

Dr. Juan Schaening

Excellent.

Karen Ravitz

Wonderful. Thank you. My name is Karen Ravitz. I am the healthcare policy advisor for the Coalition of Wound Care Manufacturers, and I do not have any conflicts of interest other than our members do pay a membership fee to participate in the Coalition. Again, I thank you for the opportunity to once again provide the Coalition's comments on the draft LCD and the accompanying LCA. The Coalition was founded in 2000, and it represents leading manufacturers of wound care products used by Medicare beneficiaries for the treatment of wounds. Our members do manufacture cellular and/or tissue-based products for skin wounds, or CTPs, which some have referred to as skin substitutes. And therefore, we do have a vested interest in ensuring that this policy is clinically sound and based on evidence.

The Coalition continues to have major concerns with these proposed LCDs. As we have previously stated, unfortunately, clinical evidence continues to be omitted from this policy review. And what is still being utilized is either not the most current evidence available or is used in such a way that is contradictory to the points that First Coast is trying to make. Furthermore, the policy continues to be fraught with clinical inaccuracies that ultimately will be detrimental to patient care. It would have been more advantageous for First Coast to reissue a draft policy which incorporated stakeholder concerns already submitted rather than reissuing virtually the same policy, but simply moving the so-called evidence recommendations out of the documentation section, as well as moving about 46 products from the covered group to the non-covered group, which is inappropriate, given this policy is still in draft form, with little to no detailed evidentiary requirements provided in the policy or any specific reasons for this change.

The Coalition once again recommends that First Coast pull this draft policy, work with stakeholders and the CAC to craft a more accurate and well-balanced policy. And as with Ms. Nusgart, the Coalition also presented oral testimony and a detailed written comment letter outlining our very expansive and substantive concerns with the draft policy, so I won't be addressing these issues again this afternoon. But I am hopeful that First Coast is hearing these comments and is seriously taking them and other stakeholder concerns into consideration as you move forward in issuing a policy.

I would like to raise a couple of specific concerns from this new draft that we find extremely problematic. As a practical matter, the MAC should not begin to enforce policies that have not yet been finalized. This is a violation of the Administrative Procedures Act. As part of the draft policy, First Coast is requesting manufacturers submit TRG letters for coverage purposes. And while TRG letters are now a requirement in order to obtain a new HCPCS code, those 361 products that have been in the marketplace for years have not been required to obtain a TRG letter. So either these products need to be grandfathered or be afforded a reasonable amount of time after this policy has been finalized to obtain these letters before any action is taken to provide non-coverage.

Furthermore, moving 46 products from the group two covered list from the original draft policy to the non-covered group three in the most recent draft list without any explanation as to why these products were moved is-- or were moved is extremely disconcerting, and it lacks in transparency. The Coalition does not support any product being included in the non-covered list until first, the policy is finalized and a reasonable amount of time has been afforded to manufacturers to obtain and submit the necessary information. This date should be in the future, after the policy has been finalized. And please note that if a letter from the TRG is being required as part of your coverage requirement, we understand that it is taking at times over nine months to obtain these letters. So until this policy is finalized with specific requirements identified, all products should still be covered as they are currently.

Second, First Coast should also identify clearly the type of evidence which is being required for coverage. I believe Dr. Lullove mentioned earlier that they should also be providing time frames, who's making the decisions, etc. Just simply stating that evidence-based literature is recommended is not specific enough. What type of evidence-based literature is First Coast willing to accept in order for a product to be placed and maintained in the group two covered list? First Coast does not provide a transparent process, and more information is needed. Third, First Coast also needs to clearly identify why products have been moved from the covered group to the non-covered group. There is no consistency in products that have been moved, and therefore, there's no clarity as to why some products were moved to the non-covered list. First Coast needs to be more transparent in the decision-making process. And as a practical matter, the LCD also says that it is recommended that manufacturers of particular CTP products obtain appropriate information and send it to the MAC along with evidence-based literature if available. Once this information has been received by the MAC, the product will be considered for coverage. So as a practical matter, doesn't this mean that the information being requested is actually being required as a manufacturer will not able to gain coverage without this submission of this material?

And Dr. Schaening, a little bit earlier, you had mentioned that the purpose of this open meeting and this new draft LCD and the movement and everything of these products was for manufacturers to submit evidentiary requirements during the comment period. But again, I'm going to say these requirements are not finalized in this policy, and they should not be required yet, until your policy has been finalized. I wanted to say thank you again for the opportunity to speak with you today. And again, based on all the significant issues contained in this policy and the substantive comments that you are hearing from stakeholders, both today and in the past, in written and oral comments, we urge First Coast not to finalize this LCD and accompanying LCA and work with stakeholders to create a more accurate and balanced policy. Thank you very much.

Dr. Juan Schaening

Thank you for your presentation. I have no questions. Does the other medical directors have any questions? Hearing none. I'm just going to make a comment. This is a proposed LCD. Nothing on this LCD has been implemented and won't be implemented until after we do the response to comment document, do the changes that we are going to do to the LCD based on the comments received, and publish the finalized LCD for 45 days' notice. So this is a proposed LCD. It's for this exact thing that we're doing, discussing it, receiving feedback, receiving comments. And we will address those comments on this additional 45 days period that we provided and then publish as-- the LCD development process requires that we should pose a response to comment document addressing all the comments received and do the changes according to the 21st Century Cures Act on the strengths of the evidence reviewed and provided. So just reassuring you that nothing on this LCD has been implemented. So let's go forward to the next presenter. The next presenter is Dr. Paul Rudolf with Arnold & [Palmer?]. Dr. Rudolf, please go ahead, stating any conflicts of interest.

Dr. Paul Rudolf

Thank you. Can you hear me?

Dr. Juan Schaening

Yes. Loud and clear, Dr. Rudolf.

Dr. Paul Rudolf

Thank you, Dr. Schaening. I'm Paul Rudolf. I'm a physician and a lawyer. My only conflict for this presentation is that I'm outside counsel for Organogenesis, the manufacturer of a number of skin substitute products that are impacted by the coverage policy. So it's been a three-hour-and-a-half meeting, and I appreciate the fact, Dr. Schaening, that you and your colleagues have had to listen to a lot of testimony and open meetings, and I would like to not be long winded. But I have to say, as a former contractor medical director myself, as someone who created hospital, physician, and coding policy at CMS for over five years and now represents many clients, including physicians, physician trade organizations, companies, I have never seen anything like this. And I'm going to say a few words, but I really hope that what comes out of this is a really constructive inside discussion among you and your colleagues at First Coast and your colleagues at Novitas to withdraw this policy and rethink it and work with everybody on this call, who are more than willing to work with you, to come up with a good policy that really helps beneficiaries.

So first, the movement of over 40 products from covered to non-covered without any explanation, without any new evidence-- we looked at the number of-- the bibliography didn't change from the original to now. So there's no new literature that was removed-- that was reviewed, I'm sorry. So how 41 products could be moved from covered to non-covered is inexplicable. There is no discussion. There is no support. And in our view, Organogenesis's view, it just seems to be arbitrary. And knowing the 21st Century Cures Act, any decision that the contractor makes, any product that's not covered, it has to be supported and discussed using evidence in the LCD.

So if we look at the evidence, the evidence actually supports coverage of all these products, and the bibliography you cite for medical society guidelines, all of which support the use of skin substitutes and do not differentiate one from the other. Most of the products on the non-covered list, there's no evidence that you review to justify non-covering them. And in particular, I point out my client's products, EpiFix, Novachor, and NuShield. There's nothing in there that supports non-coverage. Another thing is that under the 21st Century Cures Act, you can't non-cover things in an article. You can only non-cover things in the LCD. So the fact that you're non-covering things in an article to begin with is a violation of process. The fact that things were moved without explanation just compounds the matter.

Furthermore, in the non-covered list, you have multiple products which actually have TRG letters. Those products were there to begin with, and there are several products that were moved in spite of the fact that they have TRG letters. At the end of the day, what's going on here is somehow there's a presumption that without a TRG letter, all products are being used incorrectly and are not being commercialized appropriately. Well, that simply isn't true, and CMS cannot do that. You cannot assume that a product that doesn't have a TRG letter is being used inappropriately. And frankly, if it was, it would still have to be on a case-by-case basis because the manufacturers don't know how the products are being used. The manufacturers promote their products in accordance with the HCT/P regulations under the FDA, so I'm at a loss to understand that presumption, and I really hope that someone at Novitas or First Coast is going to explain why products with TRG letters are on the non-covered list.

So that just goes to the list and to the process issues going on here. But for the clinical issues, I can tell you I totally agree with the previous presenter about the amputations. I can tell you that my client is in the process of doing a claims analysis looking at claims data for patients who have similar wounds. One cohort, one group has skins substitutes; the other doesn't. We follow them for 18 months. We look at everything under the sun. And I can tell you that data, which is real-world data-- Medicare claims data that major amputations are significantly reduced in patients who have skin substitutes compared to those who don't. And that includes your jurisdiction in Florida and the Novitas jurisdictions in the Mid-Atlantic and in the Southwest. I would hope that Novitas and First Coast has done a similar claims analysis to understand the effect that these products actually have on patients.

Now, with respect to the TRG letters, you quoted the CMS final rule from last year, which I've also read very carefully. And in fact, I reread it after you made your statement. There was no requirement there that companies get TRG letters. The statement was made in the context of creating G-codes for synthetic products. And it was sort of offhand comments that went to do with coverage. There was no requirement. I agree with the previous presenter who said right now the only requirement is for manufacturers who are applying for new Q-codes, they do have to submit TRG letters. CMS has not said a word about products that currently exist, and if CMS isn't requiring TRG letters, it's not clear to me why First Coast and Novitas are, but in a final policy, I suppose you could do that. But as other presenters have said, there's no requirement for anybody to get a TRG letter until you finalize a policy that says TRG letters are required, which means if you finalize something like that, then you should give manufacturers a year to get the letters because that's how long it's going to take.

But you shouldn't non-cover products because you're presuming that they're not being used properly. I mean, this is an FDA marketing thing; it's nothing to do with whether something in an individual case is being used in a reasonable and necessary way. So as you can tell, I did submit a two-page series of talking points, which I've digressed from a little bit, but I do think that-- and myself, as a former medical director for TrailBlazer back in the day when TrailBlazer actually was currently the Novitas jurisdiction and as someone who did payment policy at CMS for five years, I really think that this is a time for everybody to take a step back for-- there's so many issues here, so many process issues. And the fact is unless in the final policy, Novitas and First Coast are willing to discuss evidence on all 150 skin substitutes and explain individually why one is covered and one isn't, it won't be compliant with the 21st Century Cures Act.

And I think that we all have to take a step back and figure out how to work together, Dr. Schaening, and come up with something that actually is good for beneficiaries, is transparent, it's understandable, and it makes sense to everybody. And we will be submitting a very detailed comment letter. And maybe Guidewell, Novitas, and First Coast would be willing to have additional meetings, but they should be in the context of a withdrawn policy. I know you understand the passion I have. All the speakers today have been passionate. And I really think that we need to somehow make lemonade out of this if we possibly can. And with that, I'll end.

Dr. Juan Schaening

Thank you for your presentation, Dr. Rudolf. Does anyone of the medical directors have any questions for Dr. Rudolf? Hearing none. Let's move forward to our next presenter. Our next presenter is Jaideep Banerjee with Smith & Nephew. Please go ahead, stating any conflicts of interest.

Jaideep Banerjee

Thank you, Dr. Schaening. Can you hear me? Dr. Juan Schaening

Dr. Juan Schaening

Yes. I can hear you very well.

Jaideep Banerjee

Okay. Perfect. Thank you very much. My conflict of interest is I am an employee of Smith & Nephew. I lead the clinical research strategy for a portfolio which includes BioTissue products and some of these CTPs. So I'd like to start by saying, first of all, thank you for giving me the opportunity to speak again. I did present comments in the last public commentary period. I think I would like to start by saying one of the biggest confusions is because some of the comments that we had put in has clearly been looked at, for example, changing the name of skin substitutes to CTPs, while others have not been addressed in this particular proposal, including two applications, right?

Now, as you have advised, we are not going to go into that in details, but my understanding is that this particular proposal is to provide time for additional manufacturers who are still in group three, and those previous comments will still be addressed by Novitas and First Coast. But having said that, I think it's necessary to hammer a couple of points which I think has not been addressed in the previous commentary period, and I'll start by mentioning Dr. Armstrong's paper that-- we have already talked about Dr. Armstrong's paper today. In addition to that, there was another paper by Dr. DaVanzo which also looked at Medicare data, and what we saw from both of those studies is that-- actually, Dr. Armstrong very clearly shows that if the physicians do not apply certain-- or some of the skin substitutes as per manufacturer's protocol, all of the benefits that you see, ED visits, cost of care, amputations-- you tend to lose all of those benefits. And both of these papers are from real-world Medicare data. Dr. DaVanzo's paper also shows effect on recurrence rates and mortality rates, right?

Dr. Schaening, you mentioned that your decisions are based purely on clinical evidence, and I really appreciate that, but as you know and today as well as in the previous commentary, we've all commented that we do not understand where this clinical evidence comes from about these two applications. There is not any FDA guidance. There is not any clinical evidence which restricts use of CTPs to two applications. In fact, most of the randomized control trials and real-world evidence points to four to six applications. So having said that, I think it's important to clarify-- if that two applications still goes forward, I think it's important to clarify what needs to be done to prepare the wound bed better for these skin substitutes because as we all understand, these skin substitutes don't become part of our skin. They help our body to regenerate, right? They help the body to physiologically react and then have the wound heal faster.

So, if that's the case, if you're restricting applications to two, then one, is there a benefit of looking into should you start application of these skin substitutes much earlier so that you don't let the wound progress to even a worse condition as you are waiting for the four week period? Is there a benefit of revisiting that and see if you can apply skin substitutes much earlier? Or on the flip side, is there a benefit to really document-- I think one of our presenters talked about this today. It's really important to either use alternative treatments or make sure that you've documented a good wound bed preparation so that when you are at that point of applying skin substitutes and you're restricted to two, that wound bed is ready to get a benefit from a skin substitute like this or a CTP like this. That'd be point number one.

Point number two would be I think what is not clear is when you're restricting the patient to two applications, is it two applications of any CTP, or is it two applications for one particular CTP, which means I think this is something that also came up in the previous commentary period. If you have an option of changing CTPs, and this is based on as the wound progresses in size and anatomy, you might be able to move from one type of CTP to another type of CTP. And are you restricting use of any CTPs on that patient to two, or is it possible to use a CTP for two applications, and maybe move on to a different or lesser expensive or a different composition kind of application, but it's still a CTP, and that also gets another two applications? I think there's a benefit in considering that.

And then finally - I think this has also been discussed a lot today - there's a national CMS policy coming up, and there's a lot of confusion because the timelines are different. So our standpoint is also that it may be beneficial to match the timelines and avoid the confusion from a national CMS CTP policy, which goes-- or for which the deadline is the end of the year, while these LCDs are intended to go or be implemented much earlier. With that, I think we will still submit these comments. And this is in addition to all the comments that we have submitted in the previous commentary. And we hope that these comments will be addressed before the LCDs are implemented.

Dr. Juan Schaening

Thank you for you presentation. They certainly will be addressed. Please submit them in writing so we may address them in our comment response document. Does any of the medical directors have a question for the presenter? Hearing none. And since there are no additional presenters for this proposed LCD, I would like to turn it back to Jan Green to provide a brief overview of the proposed LCD on intravenous immune globulin. Jan, please proceed.

Jan Green

Thank you, Dr. Schaening. This LCD has been revised to create a uniform LCD with other MAC jurisdictions. Once this revision to the LCD becomes effective, the current First Coast LCD, L34007, intravenous immune globulin, and the related billing and coding article, A5777A, will be replaced with this revised policy. Routine data analysis indicates an increase in the utilization of some immune globulin services, suggesting a need to update the LCD. The scope of the current LCD is limited to intravenous immune globulin use. The revised LCD addresses both subcutaneous and intravenous immune globulin use, providing coverage consistent with the FDA-approved indications.

The revised LCD has limited coverage of intravenous immune globulin for off-label indications where the evidence supports such use. Currently, subcutaneous immune globulin is FDA approved for use in the treatment of primary immunodeficiency disease only, except for one subcutaneous immune globulin product that is also approved for maintenance therapy in adults with chronic inflammatory demyelinating polyneuropathy. Currently, data is lacking in the literature for more widespread use of subcutaneous immune globulin. Therefore, the use for off-label conditions cannot be recommended at this time. Back to you, Dr. Schaening.

Dr. Juan Schaening

Thank you, Jan, for your presentation. Since there are no presenters for this LCD, I just would like to thank everyone for their participation in today's open meeting. And we are grateful for all your comments. And just submit them in writing before the end of the comment period, and any additional comments that you may have, please submit them in writing before September 24, 2022. That will be the end of this comment period. With this, the meeting is adjourned. And thank you all for your participation. Greatly appreciated. Have a beautiful day.