ALLIANCE OF
WOUND CARE
STAKEHOLDERS
POWER THROUGH COLLECTIVE ADVOCACY™
★CELEBRATING 20 YEARS★

April 26, 2022

K. Dev Verma
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 22, Rm. 5327,
Silver Spring, MD 20993
FDA-2021-N-1212

Submitted electronically to www.regulations.gov

Re: Wound Healing Scientific Workshop (Docket No. FDA-2021-N-1212)

Dear Dr. Verma;

On behalf of the Alliance of Wound Care Stakeholders, ("Alliance"), I am pleased to submit our comments on questions posed for the upcoming Wound Healing Scientific Workshop. The Alliance is a non-profit multidisciplinary trade association of physician specialty societies, clinical and patient associations whose mission is to promote evidence-based quality care and access to products and services for people with chronic wounds through effective advocacy and educational outreach in the regulatory, legislative, and public arenas. The Alliance is viewed as the umbrella association for all of wound care since our membership includes not only the clinical and patient associations mentioned but also wound care clinics and business entities (manufacturers and distributors). This letter was written based on the input of all our members. A list of our members can be found on our website: http://www.woundcarestakeholders.org/about/members

The Alliance is pleased to serve as a resource to FDA staff since we have worked over the years to address many issues of commonality. On July 20, 2015 we met with the FDA's InterCenter Wound Healing Working Group to discuss issues and possible update for its *2006 Chronic Cutaneous Ulcer and Burn Wound-Developing Products for Treatment* guidance document which included such discussion points as: product labels/indications; facilitate label modification to meet patient needs and foster innovation and define data thresholds for products with various risk/benefit profiles. Since many of these issues are still relevant today, I have attached the powerpoint presentation that was used in the meeting. One example is the recommendation for FDA to update its classification for cellular and/or tissue-based products for skin wounds (skin substitutes) to match the current terminology to differentiate them from "wound dressings." This was slide #25 in the 2015 presentation which we have updated and attached to this document. We will be providing additional comments on this topic and others to the Agency.

The FDA had asked stakeholders to respond in advance with answers to questions that it will pose in its Wound Healing Scientific Workshop. Since our members include wound care providers, manufacturers, wound care researchers and reimbursement experts, we are providing our initial response to these questions. These answers

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came from our recent in person meeting of 70 members where we spent a few hours discussing these questions and providing their answers below. We will submit a more detailed response after the FDA workshop and after the Alliance has had the opportunity to host our Evidence Summit May 19-20, 2022.

- ***Wound Care Provider Questions:***

a. *Wound types: What subtypes of nonhealing chronic wounds do you treat in your practice (e.g., diabetic foot ulcers, pressure wounds, arterial wounds, venous wounds)?*

Alliance members treat every type of wound. In addition to the "traditional" chronic non healing wounds/ulcers such as: diabetic foot venous, arterial and pressure ulcers/injuries, Alliance members treat wound types including but not limited to:

- Surgical
- Atypical
- Infections of the skin
- Pediatric
- Complications of burns
- Complications of traumatic wounds
- Complications of radiation for cancer (skin cancer and other types)
- Pyoderma gangrenosum
- Vasculitis
- Calcific uremic arteriopathy (calciphylaxis)

b. *Challenges: What have been your challenges to providing care to patients with nonhealing chronic wounds?*

Some of the challenges that Alliance members have encountered when providing care to their patients with non-healing chronic wounds include but are not limited to:

- Insurance coverage/reimbursement
- Getting patients the proper dressings to use at home in between visits, depending on what the provider wants and what the patient is willing to pay for
- Social determinants of health
- The inability to understand how to utilize both RCT and real-world evidence in selection of patients for appropriate therapies
- Access to supplies
- Ongoing Covid-19 pandemic
- Patient compliance
- Understanding how to improve the care of our patients so they can fit into what a clinical trial says should be the criteria that allows them to be indicated for use
- Availability of certain advanced modalities
- Working as a team with other providers regarding management of other medical conditions that affect wound healing
- Access to nutritional supplements that are proven to improve healing

- Management of underlying conditions that are the primary cause of wounds including malnutrition, heart failure and others

c. *Standard of Care: Do you utilize a standard of care protocol for your nonhealing chronic wound patients? If so, describe what standard of care protocol you utilize (specified by wound etiology).*

- The standard of care is dependent on many things. If there is a particular guideline that your practice is using as well as the type of wound being treated.
- There is no standard of care for a patient with a wound who presents at a hospital and most often, social determinants of care, impact the standard of care protocol, as do different comorbidities and place of service. While clinical practice guidelines do exist, the protocols contained in the guideline is dependent on what organization developed the guideline and also whether the facility has adopted it as part of their practice. As a practical matter, clinical practice guidelines are not accessible to the clinician at the bedside because they are usually quite long (sometimes over 350 pages).
- Some clinicians implement CMS approved quality measures for wound care including arterial screening of all lower extremity wounds and ulcers for healing potential, compression of venous ulcers, off-loading of diabetic foot ulcers and nutritional screening and implementation of nutritional interventions (see all quality measures here: https://uswoundregistry.com/quality-measures/)

d. *Products: What new products (e.g., drugs, devices, biologics, combination products) would you find helpful in treating nonhealing chronic wounds?*

The Alliance will provide more information in our more detailed response. In the meantime, Alliance members believe that they could use innovative medicines, therapies, diagnostics, and formulations. They would like to see the development of real, new technology to treat patients that are cost-effective since there is a real need for such technologies. An example of a new technology is platelet rich plasma is which will help heal chronic wounds.

e. *Reimbursement: How does reimbursement affect your ability to provide care?*

The Alliance cannot underscore enough that coverage and reimbursement impacts our clinician members' ability to treat their patients 100%. Unfortunately, the needs of the patient are not what drives care. What drives care is "what is covered and thus reimbursed." Clinicians always want to provide the best most and effective treatments for their patients – but if it is not covered or their facility will lose money on the therapy, they cannot provide it.

- ***Product Developers/Researcher Questions:***

a. *Challenges: What are strategic, operational, and tactical challenges (and possible solutions) to implementation of successful clinical trials for chronic, nonhealing wounds?*

There are several challenges to the implementation of successful trials for chronic non-healing wounds including but certainly not limited to:

- Wound care is very complex. Patients with chronic wounds have serious co-morbid conditions that distinguish them from the patients of wound care RCTs. Due to the serious co-morbidities that chronic wound care patients have (those with chronic wounds often have multiple co-morbidities such as diabetes, heart failure, chronic kidney and vascular disease, and their bodies respond differently at various times to various wound healing components) most are not eligible for participating in RCTs due to the inclusion/exclusion criteria. The USWR evaluated the exclusion criteria of all major randomized controlled trials (RCTs) performed in wound care over a decade (1998-2008). It compared those exclusion criteria with the co-morbid conditions, wound characteristics and medications documented among 3,201 patients in 18 hospital based outpatient wound centers. Its findings were that approximately 75% of real world patients would have been excluded from every major wound healing RCT that brought new products to market over that decade at the "first pass" (based on wound severity and co-morbid medical conditions) even before study related laboratories or tests would have been performed, and in fact, that RCTs enroll patients healthier than "the man on the street" based on the prevalence of the excluded conditions.

  Recommendation: The FDA issued a guidance document (*Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry (Docket FDA-2020-D-2307).* The Alliance suggests adding some resources specific to wound care in this guidance document as we continue to try to establish industry standards. As such, we recommend that the Agency reference the following articles in this guidance document:

  - Carter, Marissa; Harnessing electronic healthcare data for wound care research: Wound registry analytic guidelines for less-biased analysis. *Wound Rep Reg* (2017). DOI:10.1111/wrr.12565
  - Fife, Caroline E., Eckert, Phil M.; Harnessing Electronic Healthcare data for wound care research: Standards for reporting observational registry data obtained directly from electronic health records. *Wound Rep Reg* (2017). DOI:10.1111/wrr.12523

- The perspective of all clinical trials is at the level of the wound rather than the PATIENT.

  - For more than a decade, registry data has shown that the average patient has more than one wound. Many times, the wounds are not of the same type (multiple wound types can coexist in one patient).
  - Due to the small size of cellular products which can be afforded under package pricing and due to other reimbursement limitations, advanced therapies can only be delivered to one wound at a time and thus wounds are often treated "serially" which increases the patient's time in service.
  - Since the likelihood that any one wound will heal is inversely proportional to the total number of wounds present, it is imperative that we focus trials at the level of the patient.

- The cost of running a trial is significant – especially RCTs – which are the generally the only type of trials that are accepted by payers despite their non-generalizability for real patients. Yet, there is a lack of funding—very little if any money at NIH or any government/federal agency issued for wound care trials compared to other financial assistance to other diseases. When trials are conducted, they are funded by manufacturers and often the trials which may be good solid scientific studies are not utilized because of suspected bias.

Solutions:

- The wound care community must start developing white papers, guidance documents, publishing the evidence that does exist, to highlight that there are successful clinical trials in chronic wound care
- Given that wound care impacts nearly 15% of Medicare beneficiaries (8.2 million patients) it would seem prudent to set aside government funding for studies
- Work with FDA, CMS and private payers to allow for acceptance of RWE to be utilized in addition to RCTs in the chronic wound care space

b. Innovation: What are barriers (and possible solutions) to wound care research in the development of innovative wound care products?

- See above for challenges including lack of funding for clinical trials and even for the analysis of existing real world data and the non-generalizability of clinical trials:
- We rely on industry to financially support a lot of our studies, so the best of the best end up in these studies, because we don't want them to fail; we need more federal funding to get more quality studies that do not give the appearance of bias
- White papers, position papers are key for showing results and increasing awareness

- ***Reimbursement Questions:***

a. Acceptable evidence: What is the current acceptable evidence for coverage decisions related to wound care products (devices, drugs, biologics, combination products)?

Currently CMS (and most private payers) only use RCTs for a majority of coverage decisions for wound care products. While evidence also exists, it is constantly rejected because there is an appearance of bias because manufacturers are the ones funding the studies. However, studies cannot be run without the investment from manufacturers since no other funding is available. Furthermore, while the FDA is pushing for real world evidence and real world data, CMS has rejected studies which uses this type of data. Until there is coordination between the agencies regarding the use of RWE and RWD, RCTs will continue to be the primary type of evidence considered. However, for the Medicare population, this is not acceptable as the studies are designed in such a way with tremendous inclusion and exclusion criteria – to a point that Medicare patients being treated for chronic wounds are not really the subjects of the study. This does not benefit the government and especially the patient.

b. Challenges: What are challenges (and possible solutions) encountered in reimbursement-related decisions for wound care treatment?

One of the biggest challenges faced is that there are different requirements between the Agencies and different terminologies used for like products which end up causing issues when bringing product to market or when trying to receive coding or coverage (both of which impact reimbursement). A few examples to highlight the issue:

1. Cellular and/or Tissue Based Products for Skin Wounds (skin substitutes) – when going through the FDA – there are many pathways for these products depending on whether they are governed under 361 of the PHS. They can also obtain a 510K, PMA, BLA. Some of these products have been designated as devices while others, biologics. Some even obtain the classification of a wound dressing, yet they are not a

dressing. When these products are cleared by the FDA and then manufacturers apply for HCPCS codes from CMS, CMS often looks to the FDA label and as a result has at times confused these CTP/skin substitute products as a wound or surgical dressing.

2. As stated above, the FDA is moving towards the acceptance of RWE/RWD for clinical trials. However, CMS and private payers will not accept this type of data for wound care products. They have repeatedly stated they would only accept RCTs. Manufacturers of innovative products/technology will not conduct one type of trial for the FDA and then another for CMS or private payers. Given that coverage is dependent on clinical evidence (and thus reimbursement potential), they will not conduct two trials since it is at a huge expense to them. Rather, they will conduct the trial that will allow for coverage and payment – despite the fact that these types of trials, given the inclusion/exclusion criteria, do not represent the Medicare population being treated.
3. Coverage and implementation of coverage policy are always at the level of the wound and the average patient has more than one wound. While CMS writes coverage policy at the "wound" level, it's analytic and auditing capabilities are at the level of the PATIENT which may make it appear that products and services are over-utilized when in fact, policies are being followed.

Solution: We need to bring together the FDA, CMS, and commercial payers to agree on clinical trial standards so they can be used in patient care settings and we need to create similar terminology when used to describe products.

Solution: We need to work with the FDA to update its classification for cellular and/or tissue-based products for skin wounds (skin substitutes) from to match the current terminology to differentiate them from "wound dressings."

Furthermore, in many cases, the third-party payer says they will pay for a wound care product/service if it is medically necessary; oftentimes, there's no clear definition on what "medically necessary" is, which can be frustrating to providers and manufacturers. As a result, sometimes what a provider believes is a medically necessary need for a particular product/service is denied as not medically necessary. This too needs to be addressed.

Finally, more reimbursement needs to be carved out for patients in skilled care under consolidated billing.

We appreciate the opportunity to provide the answers to these questions. As stated previously, we will provide to the Agency a more detailed response after the FDA workshop and after the Alliance has had the opportunity to host our Evidence Summit May 19-20, 2022.

Sincerely,

Marcia Nusgart R.Ph.
Executive Director