Collagen Dressings in Chronic Wound Healing

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ADVERTISING & PUBLIC RELATIONS

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Introduction

To properly position Collagen Dressings as they exist at the present time, it is useful to briefly review the development of accepted thought and practice applied to wound healing over the past few decades.

Until the work of Winter in the ‘60s (1962), dressing acute and surgical wounds followed the practices dictated by the community of surgeons and their associates and assistants.

Wounds were covered with dry or slightly moistened gauze dressings that were changed up to 3 times per day.

The goal was to “cover and protect” the wound, and to prevent infection at all costs through the use of antiseptics and the multiple dressing change regimes.

Approached like battlefield injuries, there might be aggressive debridement up front, but keeping the wound clean and dry was the normal state of affairs.

In the case of acute wounds with healthy perfusion, healing was routine no matter what wound treatment protocol was employed. The differentiation between chronic and acute wound care often revolved upon who was assigned to manage the chronic wounds where the rewards -- both financial and professional -- were few. Surgeons would impose the dry gauze TID routine common to their professors’ idea of wound care, where those working with chronic wounds every day were more creative.

Protocol: Dressings dry, frequent dressing changes, slightly modified procedures from acute wounds.

Winter introduced the controversial concept that wounds might heal faster and with fewer complications if the wound bed was left somewhat moist.

Winter’s early work demonstrated that a scabbed wound, when covered with a transparent, occlusive cover generated fluid that softened the scab, leading to its being liquefied (starting from the edge, working in). This resulted in the scab gently detaching from the wound bed.

It appeared that the moist wound condition actually supported a mechanism where natural physiological processes were stimulated and supported in such a manner that debridement occurred (autolytic debridement), followed by a demonstrable reduction in the time it took for wounds to heal.

This work introduced the ideas that no physiological processes naturally occur in a dry environment, and that (like the moist conditions under a blister) there was a natural sequence progression to healing that required moisture for healing to progress.

The power of this logic was evident to a growing number of wound researchers, and the concept was applied to both acute and chronic wounds with great success.

Early converts took great pains to create their moist wound environment, which at that time involved sealing films like Saran Wrap over the wound bed and allowing fluid to accumulate. If fluid accumulated too rapidly to allow the dressing to remain in place, it could be drained by puncturing the film with a needle and drawing out the excess, then patching the hole to get a few more hour's or day's use out of the dressing.

Not all clinicians immediately assumed the trapped fluid was a good thing. Many worried that it may, In fact, be pus to be removed to avoid infection. Those who persevered past the pus misconception saw that, rather than a detriment, the natural wound fluid possessed properties that appeared to greatly benefit the patient and the wound.

As more clinicians became interested in investigating and applying moist wound technology, the method of creating that environment evolved from taping non-occlusive films to the introduction of films with pre-applied adhesives.

The producers of transparent surgical drapes found their large products being chopped up and employed to cover smaller wounds. The adhesive transparent dressings had the advantage of convenience (just apply over the wound and the dressings stick to the peri-wound skin) and improved safety as they protected the periwound skin form maceration and digestion by wound fluid.

An interesting aside: those making the surgical drapes almost missed out on participating in the wound care evolution due to the massive resistance of their operation's executives, who could not imagine why they should waste time or money making smaller "drapes," as obviously there were no surgical procedures (no endoscopic/ minimally-invasive surgery at that time) that required small drapes.

Tiny transparent drapes were inconvenient to manufacture and required additional steps and packaging.

Smith + Nephew (S+N) was first-to-market, and found their OpSite (the name was derived from "Operation Site") adhesive transparent film dressings were rapidly adopted for holding IVs in place, as well as for use as "occlusive" surgical dressings.

Others quickly introduced similar produces, and S+N enjoyed many years of royalties from 3M and Johnson & Johnson (J+J) for use of their patents.

Unlike S+N, however, 3M and J+J, were much faster at improving the practical aspects of film dressing use, especially in perfecting the delivery systems (OpSite was tricky to apply).

3M's Tegaderm with a window delivery system and J+J's Bioclusive essentially out-competed S+N until they finally introduced more practical versions of OpSite.

During this period, application ease was king, followed by comparisons of performance and the toxicity of the adhesives employed.

Concept and science are not enough: products must be easy to use.

Film dressings demonstrated the superior characteristics of Moist Wound Healing (MWH – Advanced dressings), and interest in the concept expanded.

The makers of Ostomy appliances realized that the Hydrocolloid wafers used to hold their ostomy appliances in place had many characteristics that could be applied to the MWH technique.

Hydrocolloid wafers remained adhered to the skin for several days, and had the advantage of being able to absorb a moderate amount of wound exudate. This property allowed them to stay on the exuding wound far longer that the film dressing. Use of MWH concepts became that much more practical.

It was often the Enterostomal nurse who oversaw the management and training of Ostomy patients, and who were, by coincidence, often tasked with the management of recalcitrant wounds others did not wish to address.

A great deal of their working day could be taken up with the dressing and redressing of chronic wounds, and they became intimately familiar with the painfully-obvious deficiencies of the wound "management" protocols in effect.

Open to new concepts, ETs were also familiar with hydrocolloid technology, and Ostomy product manufacturers targeted this enthusiastic and caring niche, convincing them to try the new hydrocolloid dressings.

Results were immediate and significant. The ET was able to reduce the number of dressing changes, and the reduced cost and painful inconvenience of the traditional approach were immediately apparent and dramatic.

Hydrocolloids provided a means to create the moist wound environment, with the ability to absorb fluid, swell to conform to the wound bed, and protect the periwound skin.

This provided the moist wound healing believers with an extremely convenient manner to practice the concept.

As Enterostomal Therapists tasked with managing chronic wounds were intimately familiar with hydrocolloid wafers, pastes, powders and adhesives, they were a natural group to "experiment" with the new concept. All would state "wound healing is an art," and many developed elaborate protocols to maintain a moist wound environment for their patients.

Articles describing benefits of transparent film and hydrocolloid began appearing in the practical journals, and the Ostomy manufacturers began promoting their products to wider audiences.

ETs described their experiences, reporting:

- Fewer Dressing changes
- Faster dressing changes
- Less pain for the patients
- Faster wound healing
- Autolytic Deridement

Moist Wound Healing's (a new and powerful factor) "scientific" approach supported the normal physiology of wound healing, and ETs rapidly became the missionaries spreading the faith in MWH far and wide. Obstacles in their quest to expand the use of moist wound healing included:

- A higher cost-per-dressing vs. traditional gauze
  - "Why should I pay $1.00 when gauze in 5 cents?"
- The accumulation of a thick "Pus-like" material under hydrocolloid dressings
  - "Oh my goodness that looks like infection!"
- A characteristic odor occurring with hydrocolloid dressings
  - "Smells like something might be wrong"
- Occasional dressing failure / leaking
  - "Gooey, stinky mess"

Administrators hated the high cost-per-dressing, and feared legal action for hospital-acquired infection.

ETs and dressing manufacturers worked to show that reducing the number of dressing changes greatly reduced the nursing cost and total cost of treatment.

Faster time to healing reduced treatment cost, as did the reduced frequency of other complications (accidental drying out of dressings).

Great effort was expended to demonstrate that the "pus" under the dressing (in the absence of any signs of infection – heat, redness, swelling, and pain) was, in fact, associated with reduced incidence of infection.

ETs in general possessed a high degree of empathy for their patients, and appreciated their new-found ability to reduce the pain associated with wound care and improving the quality-of-life for their patients.

It is interesting to note that, at this time, most of the sales of what came to be known as "advanced wound care" products were being driven by nursing staff, especially the ET.

Surgeons and other specialists had no financial interest in chronic wounds, and often considered them as medical "failures." They were happy to abdicate treatment responsibility to the ET and leave the details up to them.

If the ETs was successful, they gained prestige and influence within the institution.

ETs were extremely happy to find there were ways to improve on the primitive, painful and time consuming traditional protocols (wet-to-dry gauze debridement), and as more chronic wound care was defaulted to them, they enthusiastically tried new options and adopted those that worked for them.

The subject of chronic wound care was added to the ET's school curriculum, and Symposia were introduced (WOCN and SAWC) where the new wound care techniques and products were discussed and promoted.

An idea of the power associated with the evolution of advanced wound care can be glimpsed by considering a before and after scenario.

Before MWH, if a wound needed debridement, a surgeon interested in the task had to be located and an operating room or a specialized treatment room had to be booked.

Surgical debridement required anesthesia and recovery, and the time interval between the decision that debridement was necessary to the time the wound was actually debrided could be weeks.

After MWH, the ET could note the wound needed debridement and apply a hydrocolloid dressing (before calling the surgeon).

After a few days, it would be apparent that the wound was using its exudate to digest the necrosis on its own through the process that became to be known as autolytic debridement.

In a great number of cases, the ET was thus able to effect debridement using only appropriate dressings (maybe a little assist from sharps), avoiding the cost, pain, and inconvenience of calling in the surgeon. (As an aside, the ET began to avoid 'surgeons' at all costs, as they were rarely up to date with MWH technique and would often order gauze packing and wet-to-dry dressing changes that were now utterly distained by the informed practitioner).

Such successes became the subject of journal articles, and presentations at scientific symposia fueled interest in MWH.

As success with MWH grew, the deficiencies in the state-of-the-art MWH products became more apparent.

The transparent film producers addressed the difficulties applying the early products with mechanisms to hold the films flat until they contacted the skin.

The hydrocolloid manufacturers changed from formulas that were great for holding ostomy appliances in place, to new formulations that addressed the needs of the wound care professional.

ConvaTec introduced its Control Gel Formula (DuoDerm CGF) with a high degree of crosslinking between the components. This resolved the loose, often odiferous residue previously experienced at dressing changes, and immediately removed several barriers that had limited the expansion of the products to new users.

As acceptance of the concept of MWH expanded, discussion and product development turned to more practical methods and materials to facilitate its use. The range of Advanced dressings expanded to include Foam, Alginate, Hydrogel, wound contact layers and specialty absorptive formats.

While early product promotion followed the pharmaceutical theme of “my ingredients are better than yours,” practical competition at this stage in fact revolved around “my product is easier to use than yours.”

From the “house dressing” used at all stages of the healing process, specialty dressings evolved based upon their ability to manage exudate, and the physical shape of the wound.

Ideal Dressing

The concept of the “Ideal Dressing” was forwarded to crystalize the thought processes of the time.
Ideal dressing, proposed by Winter 1975 (after Scales 1956), would have the following characteristics:

1. Good absorption of blood and exudate
2. Sterilizeable
3. Non-toxic
4. Non-allergenic, non-sensitizing
5. Constant performance over a range of temperatures and humidity
6. Non-flammable
7. Small bulk (reduced storage space requirement)
8. Long shelf life / stable
9. Conformable to anatomical contours
10. Tear-resistant
11. Creates moist wound microclimate (oxygen permeable, prevents dehydration)
12. Provides barrier to secondary infection
13. Non-adherent
14. Fiber-fast (does not shed loose material into the wound)
15. Provides mechanical protection to the wound
16. Soil-resistant
17. May accept and release medicaments (drug delivery)
18. Cost-effective

Dr. Thomas, former director of The Surgical Materials Testing Laboratory, points out that the first 10 ideal properties may be provided by traditional dressing; however, the next ideal criteria require the use of “advanced” dressing materials.

Post-2010 dressings include additional “ideal” criteria consistent with advances in the understanding of wound healing, and the practical observation of dressing performance.

Exudate Management

Having accepted that some dressings are better than gauze, WC practitioners established criteria to guide them in selecting the new dressings.

The two most successful selection aids were the Molnlyke RYB (red yellow black), referring to granulating, sloughy or necrotic wound stages, and the S+N-championed Wet/Dry, Shallow/Deep model.

Molnlycke color coded their dressings to make it easy to select an appropriate dressing based on wound color (indicating state of healing), where S+N suggested a selection protocol based first on the amount of wound exudate, followed by consideration of wound depth (plus undermining).

The Moisture/Depth matrix was useful to both practitioners and manufacturers alike, as it clearly pointed out what type of products were needed to cover all wound types encountered.

Moisture

Transparent films were excellent at remoistening dry wounds, but could not handle significant exudate.

Hydrocolloids provided an improvement on managing more exudate, and suggested that there was a need for materials that could manage wounds when hydrocolloids failed.

Material	Exudate
Transparent film Standard MVTR or High MVTR	Dry/Low
Hydrocolloid wafer Thin, regular, thick	Low/Moderate
Hydrocolloid pastes/powders	Moderate to High
Foam dressings	
Pad	Moderate to High (Hydro Active)
Pouch	Moderate to High (Foam chips in a pouch)
Alginate Dressings (now including Hydrofiber dressings)	
Pad	Moderate to High
Rope	Moderate to High

Hydrogels		
Sheet	Low	
Amorphous	Low	
Hydrogel saturated	Low	
Specialty Absorptive	High	Recently introduced Superabsorbers and“hydroconductive” (Drawtex)
Wound contact layer	All	Moisture passes through to cover dressing

New materials such as polyurethane foam dressings, alginates and hydrogels were introduced in an attempt to match dressing absorption performance to the level of exudate generated by the wound.

In this manner the moist wound environment could be created (hydrogels) or maintained (foam, alginates, super-absorbers) for longer periods between dressing changes.

Increasing the period between dressing changes is instrumental in:

- Reducing cost (fewer dressings, reduced professional time)
- Increasing healing, less disturbance to the healing process
- Improving quality of life
- Less dressing change pain
- Fewer changes

All dressing materials used to create “advanced wound dressings,” to this point, were synthetic (polyurethane foams and films) or plant-derived (alginate, carboxymethyl cellulose/CMC).

Use of animal derived materials such as collagens or other ExtraCellular Matrix (ECM) materials was non-significant.

Depth

The second practical criteria for dressing selection related to the need to fill the open or “dead space” with material to help maintain limb shape and to maintain an intimate contact between the dressing and wound bed surface.

Dressings without fixed dimensions able to pack open space were introduced and rapidly adopted for their practical utility.

Alginate dressings provided a significant improvement in wear time over hydrocolloids, plus they could be used to pack undermined areas (in rope form) or stacked to fill deep cavity wounds.

Hydrogel sheets conformed exquisitely to shallow wounds, while amorphous addressing and saturated hydrogel dressings worked well to pack deep and undermined, minimally-exuding wounds.

	Exudate	Depth
Transparent film	Dry/Low	Shallow
Hydrocolloid wafer	Low/Moderate	Shallow
Hydrocolloid pastes/powders	Moderate	Deep/Undermined
Foam dressings		
Pad	Moderate/High	Shallow/Moderate
Pouch	Moderate/High	Deep
Alginate Dressings (now including Hydrofiber and Drawtex types)		
Pad	Moderate/High	Moderate/Deep
Rope	Moderate/ High	Moderate/Deep/Undermined
Hydrogels		
Sheet	Low	Shallow
Amorphous	Low	Moderate/Deep
Hydrogel saturated	Low	Shallow Moderate/Deep
Specialty absorptive	High	Shallow, Moderate/Deep (with Packing)
Wound contact layer	All	All

(Note: there were no antimicrobial dressings at this stage. At this point, dressings differentiated as to those cleared for use on infected wounds and those without that claim. Infection was managed by debridement, wound cleansing, antimicrobials and antibiotics.)

Collagen Dressings were later introduced to participate in the low-exudate/moderate-depth segment (except Fibracol), with sheets and pads and in the high-exudate/deep-wound niche with flakes and powders. Low exudate-deep wounds might be addressed with Collagen Hydrogels.

Wound Care Science

While a great deal of effort and design was invested in delivering ever more practical moist wound dressings, a great deal of research and publication was accumulating on to the science of what was going on during the process of wound healing. The science supported the use of the moist wound healing paradigm, and suggested mechanisms for improvement of advanced wound care protocols.

Most discussion of the science behind wound care began with the phases of wound healing as applied to acute wounds.

Current understanding of the healing physiology is applied to each stage, and some differentiation between acute and chronic healing is applied.

Phase 1: Hemostasis ("plug the hole and bring in the Cavalry")

The first and shortest (in terms of days) phase of healing after acute injury is Hemostasis.

Injury to the Extracellular Matrix (fibrillar collagen) serves as stimulus to activate local platelets. Platelets secrete a mix of cytokines to attract more platelets, activate the intrinsic clotting cascade, and form a plug to stop blood loss.

The platelet population then signals for the accumulation and activation of Macrophages and other inflammatory cells (Neutrophils, PMNS) which generate the signals necessary to begin and support the next (inflammatory) stage of wound healing.

In chronic wounds this step may be missing or modified, leading to a lack of proper signaling. For example, neither pressure ulcers nor venous leg ulcers pass through a stage of obvious bleeding that would require hemostasis and the robust activation of platelets analogous to that seen in acute wounds. (Wound care practitioners may address this issue by starting wound treatment with extensive surgical debridement in an attempt to shift the wound healing trajectory from chronic to acute.)

Platelets aggregate around exposed collagen, suggesting that components of the extracellular matrix may play a role that could be exploited in organizing chronic wound repair (introduce exposed collagen, collagen fragments early in the healing process).

Oxidized Regenerated Cellulose/Collagen (ORC), collagen sponges, or alginates may be used as Hemostatic agents to stop bleeding.

Hemostasis

The epidermis provides the first barrier of protection from the invasion of foreign substances into the body. The principal cell of the epidermis is the keratinocyte. The dermis (the layer just below the epidermis) assumes the important functions of the thermoregulation and supports the vascular network to supply the avascular epidermis with nutrients. The dermis contains fibroblasts, which are responsible for secreting collagen, elastin, and ground substance that give support and elasticity to the skin. Immune cells are also present and defend against foreign invaders that pass through the epidermis. The hypodermis, also called the hypoderm, subcutaneous tissue, or superficial fascia, is the lowest layer of the skin. Types of cells found in the hypodermis are fibroblasts, adipose (fat) cells, and macrophages. Upon injury, a series of biochemical events are initiated. These activities are generally grouped into 4 overlapping phases (hemostasis, inflammation, proliferation, and remodeling).

Phase II: Inflammation ("Clean out the wound. Remove non-viable tissue and contaminants.")

The second phase of wound healing may be understood as the process of cleansing the wound of barriers to healing, and preparing it for repair.

During this phase, exudate is generated that serves to flush out loose debris and lightly attached necrosis. The exudate contains a wide array of cells and biochemical agents that are harnessed under moist wound dressings to degrade necrosis and vectors of wound infection.

Macrophages and other inflammatory cells communicate to coordinate their activities through chemical mediators called cytokines. Damaged tissues are identified, and enzymes specific to the Extracellular Matrix (mostly collagen) are secreted to digest and remove them from the area.

Many of the enzymes include a zinc atom and are referred to as Matrix Metalloproteases or MMPs (proteolytic enzymes with a metal component that digest the extracellular matrix).

In acute wounds, the activity of the MMPs digesting damaged tissue is closely regulated by the secretion of TIMPS (tissue inhibitors of MMPs).

In chronic wounds, the inhibition appears to be less than perfect, and digestion of healthy ECM and newly forming ECM may create a positive feedback loop that leads to more production of the substances that induce MMP production and those that stimulate inflammatory processes.

Proteolytic enzymes breakdown ECM, and the breakdown peptides (collagen and other protein fragments) have a chemotactic effect, resulting in the recruitment of more inflammatory cells and an increase in digestive enzyme production.

In this manner, chronic wounds are kept in a constant inflammatory state, and are unable to complete the process of wound bed preparation necessary for the wound to move on to the next (constructive) phase of healing.

Healing will not take place in a manner that would cover damaged tissue, debris, microbes (now biofilm), and such materials must be removed through natural processes or by extensive cleansing and debridement.

MMPs themselves as well as certain ECM breakdown products and immune complexes (unresolved microbe issues) perpetuate the inflammatory phase of healing.

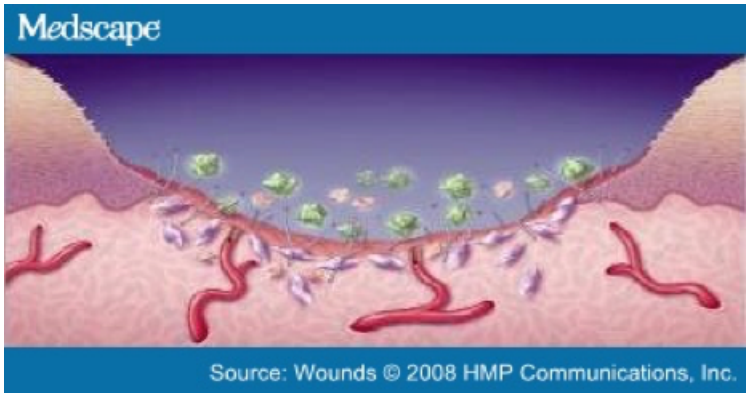
As collagen has been linked to the generating of many of the pro-inflammatory mediators and MMPs (Cullen's cycle), several strategies involving collagen have been described and employed to reduce inflammation.

It should be noted that the shift from one phase of wound healing to another is not abrupt nor coordinated across the entire wound surface.

Parts of the wound may have left the inflammatory phase while other parts are at the tipping point where tissue destruction is barely matched by tissue regeneration, and other parts may be stuck in inflammation with no progress towards healing.

Hemostasis: Plug the hole and bring in the Cavalry

Inflammatory: Cleanse the wound of damaged ECM, cells (necrotic or sloughy tissue), debris and microbes and prepare the wound bed for repair.



Initially, macrophages act to remove the cell debris and bacteria. They secrete cytokines and growth factors, which guide the wound through the inflammatory phase into the proliferative phase. Endothelial cells (tan-colored cells) create new blood vessels. Fibroblasts (purple colored cells) produce collagen a key component of the extracellular matrix (ECM) and secrete matrix metalloproteinases (MMPs), tissue inhibitors of matrix metalloproteinases (TIMPs), and glycosaminoglyacans (GAGs). Glycosaminoglyacans bind with water to create a gel medium, which aids in cell movement.

Macrophages secrete pro-inflammatory cytokines (eg, TNF-α and IL-1α), which signal fibroblasts to secrete MMPs (orange colored cells), TIMPs, and GAGs. The MMPs degrade the nonviable collagen to prepare the wound bed for granulation. The degradation products are chemotactic agents, which stimulate migration of fibroblasts, epithelial cells, and vascular endothelial cells. TIMPs inhibit MMPs to a certain extent to assure the level of activity of the MMPs remains at the optimal level for wound healing.

Fibroblasts secrete new fibrous proteins, such as collagen and GAGs. The fibrous proteins act as a scaffold upon which cells can migrate. Glycosaminoglycans and the fibrous proteins make up the ECM. Endothelial cells create new capillaries. The granulation tissue provides the surface for Migration of keratinocytes to cover the wound.

Phase III: Proliferation/Granulation ("Fill the hole and restore structure [granulation, epithelialization] to produce scar tissue.")

As the wound is cleansed through inflammatory processes, there is a reduction in the creation of inflammatory mediators and tissue breakdown product.

Macrophages induce the accumulation and proliferation of Fibroblasts, which become the dominant cell in the repair process at this stage. Fibroblasts generate replacement collagen and other ECM components, and release a variety of growth factors that promote angiogenesis and the production of granulation tissue to fill the wound with living tissue.

Enzymes are employed to prepare the wound surface for keratinocyte migration and proliferation to eventually cover the wound with epidermis.

Substances are laid down quickly, modified and utilized for the stimulation and coordination of repair.

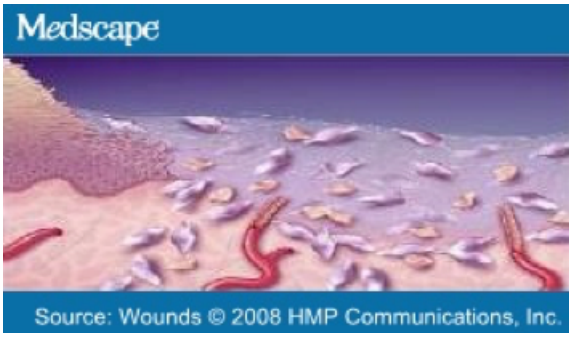
Collagen represents 75% of the ECM, and the ECM has been implicated in guiding regenerative cells into proper position.

Collagen cleavage products have been implicated in the stimulation of keratinocytes, and many of the newer "dressings" rely on collagen to provide shape and other properties (reservoir for growth factors, attachment points for migrating cells) to stimulate, organize and speed up the proliferation processes.

Hemostasis: Fill the hole and bring in the Cavalry.

Inflammatory: Cleanse the wound of damaged ECM, cells (necrotic or sloughy tissue), debris, microbes and immune complexes.

Proliferation: Plug the hole. Generate replacement ECM, capillaries and cells to replace missing tissues. The repair is highly vascularized (granulation tissue) and does not contain the variety of tissues and cells found in normal tissue. It is referred to a scar tissue.



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Phase IV: Remodeling ("Rework the quick plug to produce a better functioning scar.")

In the acute wound, the process of healing progresses quickly with the fast clot followed by inflammatory cleansing and proliferation of a more permanent plug (scar).

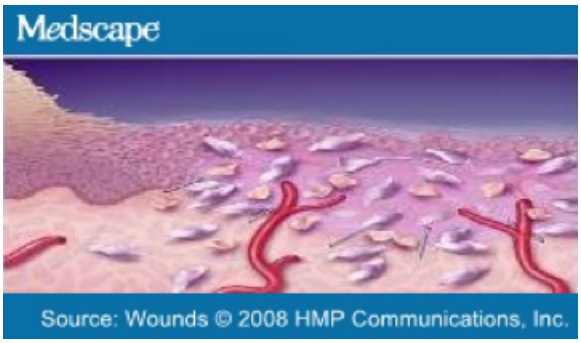
The quick plug serves its function, and then is remodeled to improve its characteristics to more resemble normal skin.

The type and orientation of ECM and extensive vascular network created to quickly plug the wound is slowly broken down and replaced with a less vascular, better organized, more supple and stronger scar.

In the chronic wound, a similar process occurs and may last much longer and with less satisfactory results.

Remodeling is the embodiment of how the body balances the catabolic (destructive) processes necessary to remove inadequate tissue, with the anabolic (constructive) processes of replacing tissue.

Healthy remodeling uses the breakdown products from the original scar to stimulate and direct their replacement with more refined and structured tissue.



Keratinocytes move across the viable granulation tissue in the process of re-epithelialization. Re-epithelialization will continue until the epidermis is continuous. In the next phase of healing fibroblasts will remodel and cross-link the collagen fibers to make a stronger more flexible scar.

Collagen:

Collagen is the main structural protein found in the body.

Proteins are a class of organic molecules, composed of long chains of amino acids (Amino group = NH2 plus hydroxyl group COOH plus variable side chain).

The function of a protein is dependent not only on its composition, but also on the shape the molecule takes and its association with other proteins, elements and molecules.

The production of collagen is dependent on the availability of Vitamin C and the nine amino acids that cannot be synthesized in the body (phenylalanine, valine, threonine, tryptophan, methionine, leucine, isoleucine, lysine, and histidine-essential amino acids), which must be supplied by diet or supplement.

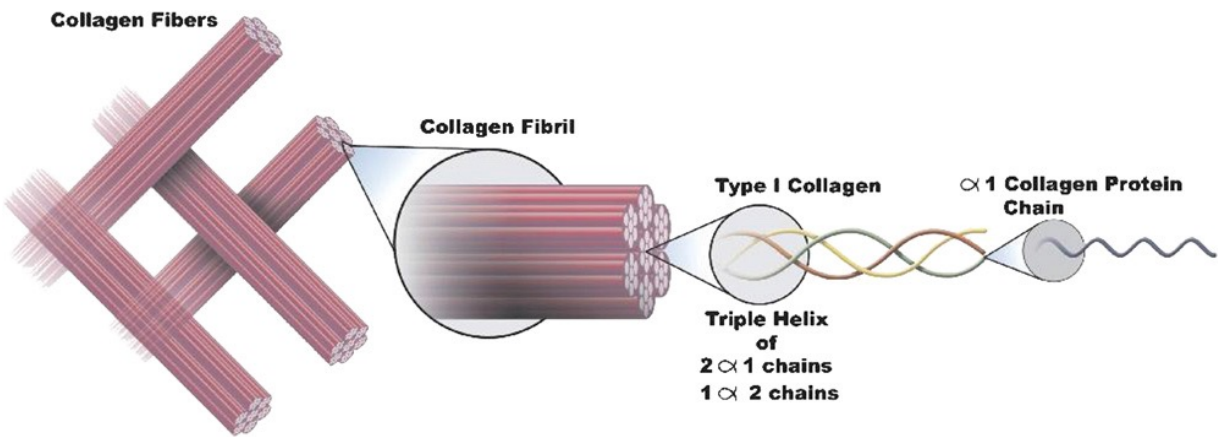
Collagen occurs in many places throughout the body. Over 90% of the collagen in the body, however, is Type I.

So far, 28 types of collagen have been identified and described. They can be divided into several groups according to the structure they form:

- Fibrillar (Type I, II, III, V, XI) -- Most employed in wound care
- Facit (Type IX, XII, XIV)
- Short chain (Type VIII, X)
- Basement membrane (Type IV) -- Utilized in composite products and some CTPs
- Other (Type VI, VII, XIII)

The five most common types are:

- Type I: skin, tendon, vascular ligature, organs, bone (main component of the organic part of bone)
- Type II: cartilage (main collagenous component of cartilage)
- Type III: reticulate (main component of reticular fibers), commonly found alongside type I.
- Type IV: forms basal lamina, the epithelium-secreted layer of the basement membrane.
- Type V: cell surfaces, hair and placenta



Amino acids are assembled through sequential addition by the cell organelle known as the ribosome.

For the production of collagen, 3 chains of amino acids with a characteristic helical configuration are produced and delivered to the endoplasmic reticulum for assembly into a triple helix protocollagen structure.

Enzymes are employed to hydrolyze the amino acids lysine and proline, allowing them to crosslink through glycosylation resulting in a structural twist to the left and bonding of the three peptides into the triple helical structure.

When considering wound healing, the dominant collagen component is Type 1 fibrillar collagen which is the major component of the extracellular matrix (ECM).

The ECM makes up the main 3-dimensional structure of the damaged tissue, and forms the tissue that is being created to repair the wound.

The ECM provides the structure (matrix) in which all tissue functions occur. It allows the cells to move and perform their structural and biochemical functions, and serves as a media for the storage and dispersion of cytokines, and growth factors released by cells (example Microphage or Fibroblast) that carry out wound repair.

Intact properly-oriented and populated ECM collagen is recognized by cells, and they perform normal functions regulated by its contents and character.

Damaged ECM exposes damaged fibrillar collagen which triggers an array of chemical and cellular responses. Damaged collagen is removed though digestion utilizing MMPs and is replaced by newly synthesized collagen. The balance between digestion and replacement is moderated though Tissue Inhibitors of MMPs (TIMPs).

Many of the signals coordinating wound cleansing (removal of damaged materials) and repair are induced by breakdown products of collagen digestion.

Activation of inflammatory cells by exposed fibrillar collagen results in (among many other processes) the release of MMPs that begin digestion of the damaged ECM.

Breakdown products generated by the digestion stimulate the accumulation of additional Macrophages and the release of additional MMPs, accelerating the removal of the injured tissue.

Macrophages may phagocytize and remove breakdown products, and as the amount of inflammatory mediators is reduced Fibroblasts release TIMPs to deactivate MMPs and allow the accumulation of replacement ECM.

New ECM provides the scaffold/matrix utilized by Fibroblasts, and endothelial cells to migrate outwards to create granulation tissue to fill the deficit.

In the Acute wound, the sequence of removal and repair events proceeds from stage to stage in such a manner that the wound heals in a predictable, positive fashion.

In the Chronic wound, several events and processes have been identified that interrupt the normal sequence of repair events and impede the wound from healing.

Many other molecules, cells and processes are involved during inflammation and proliferation and the creation and deposition of a functional EMP properly vascularized (granulation tissue), filling the wound bed to the level where re-epithelialization is possible is dependent on the coordination of hundreds of events in space and time that must come together to effect repair.

Interest in Collagen as a wound dressing follows consideration of the many ways collagen and its derivatives are involved in wound repair.

Collagen

- Main component of the ECM by volume
- Hemostatic properties
- Initial stimulus for wound healing cascade
- Breakdown products have major regulatory function
- Provides scaffold for cell migration
- Provides reservoir and media for dispersion of cytokines and growth factors.
- Many formats are bio-absorbable and do not need to be removed

Collagen Sources

- Human Biosciences USA
- Collagen Corp USA
- Sigma-Aldrich International
- Covalon Canada
- Collagen Solutions Scotland
- Euroresearch Italy
- MiMedx USA
- Suweleck Germany

Collagen Dressings: Evolution

Overview: Bottom Up / Top down

The evolution of collagen dressings has proceeded from two directions.

The first is from consideration of collagen as an addition to the advanced wound care dressing materials continuum, as a natural addition to the materials used in creation of moist wound healing dressings.

The second is from consideration of full-thickness skin grafts leading to the processing of intact tissues to create a simplified regeneration templates.

In the first instance ("bottom up"), a solution of collagen (Collagen in Solution, or "CIS") from any of a variety of animal sources is prepared and utilized as the starting material to generate a dressing.

In the second instance ("top down"), tissue such as sheep stomach lining, sub-intestinal submucosa (SIS), or more autologous sources (human placenta or dermis) is processed in such a manner that a simplified matrix with cells and other immunogenic materials removed is produced, leaving a more natural structure for regeneration.

Starting with actual tissue and removing selected components (immunogenic components) provides a higher chance that the matrix is physiologically appropriate (space for new capillaries, attachment points for cell migration), without having to understand it while the bottom up approach lends itself to much variation as new key elements are discovered.

Early collagen dressings were created by filling shallow vessels with collagen dispersions (CIS) of various sources (avine, ovine etc.), such as Vitogen from Collagen Corp., and inducing collagen precipitation through manipulation of pH.

This process produced cast collagen sheets of fibrillar collagen. Cast sheets were flash frozen (to minimize ice crystal production and size) and freeze dried (lyophilised) to create 3-dimensional, sponge-like materials. The sheets could be further processed to create power/flake/particle formats, or collagen gel dressings.

By varying the details of production, the properties of the dressing could be directed toward desirable characteristics:

- Low collagen concentration – easier to tear, faster degradation in the wound
- High collagen concentration – denser structure, stronger, slower degradation
- Pore size, (introduce bubbles/gas) to regulate the ability of cells to enter or be exluded from the dressing
- Additives
  - Add GAGs to improve moisture mmanagment and cell interation
  - Add Alginates for increase absorption capacity
  - Add ORC for mosture, flexibilty and Improved MMP and GF interactions
  - Add EDTA to permantly deactivate MMPs

Additives can be included in the pre-precipitation solutions (in the CIS), where they may be incorporated into the 3-dimensional structure of the sheet, or they may be added by soaking the dressing post-production (drugs, GFs, Cytokines, Silver).

CIS may subjected to various types and degrees of crosslinking that significantly affects the final properties of the products.

The number and location of the cross links will determine resistance to degradation by MMPs, affecting dressing durabilty and the nature of the breakdown products produced, and their subsequent effects on the wound environment.

Several patents have been filed protecting methods to direct and limit crosslinking character to generate desireable wound care properties. Continuous sheets without a pore structure can be left as occlusive dressings or can be fenestrated to allow the passage of exudate.

Collagen may also be processed by a process similar to digestion, where its long chain structure is esstially hydolized (choped up) into smaller components. The prouct produced by this method is generically refered to as gelatin.

Much marketing material is dedicated to the premise that Native (un-hydrolized) collagen is more “natural” and therefore more appropriate for wound healing.

It is stated that the MMP attraction and function is more natural with native collagen, producing a more robust heaing respnse.

On the other hand, those touting the use of gelatin (hydrolized) product claim that their state of collagen is predigested, making it easier and more natural and more efficient for the wound physiology to interact with the components released by the ‘activation’ of collage.

More fragments mean more active sites and more physiogical activity (good or bad?). The argument for Native collagen appears to be taking the upper hand for now; however, the continued use of both suggests there may not be a single answer that is appropriate for all wounds at all stages of healing.

Collagen dressing development summary

Traditional Dry Dressings: Passive, before collagen dressings/early collagen hemostats

- Work fine for acute wounds (will heal despite bad procedures)
- High frequency of dressing changes
- Fight to avoid infection.
- Hemostasis natural or SurgiCel (Oxygenated Reconstituted Cellulose ORC)

Advanced Wound Care Dressings: Passive, Collagen promoted as a logical MWH substrate

- Use of occlusion to concentrate wound fluid
- Release healing power of natural physiology in moist environment.
- Manage exudate (Sheet, Powder, Gel)
- Fill dead space (Powder, Gel)
- Support Moist Wound Healing
- Collagen “bottom up” as basically a new MWH substrate
    - Process
        - Lyophilized, sponge with pores (see photo)
        - Native
        - Animal - Ovine, Porcine, Avine
    - Claims started just reiterating MWH claims
        - Forms a gel
        - Supports MWH
        - Early claim as ‘scaffold’ BUT removed scaffold every few days (with the good stuff)
        - Add Alginate to increase absorption and gel forming character
    - FDA 529(k) Restrictions
        - Cannot label for use in 3rd degree burns
        - Cannot label improved / accelerated healing
        - Cannot label long term or absorbable
        - Cannot label for treatment or cure of any wound
    - 1st use of animal sourced material as main component of wound dressing (previous dressings used synthetic or plant-derived substrates)

Collagen as Biological: Active, plus additives

- Scaffolding story expanded Purpose to structure
- Some ease on restrictions as absorbable
- Introduced ORC as modifying MMPs and GFs
- Introduced EDTA as irreversable MMP inactivator
- Promoted active sacrificial substrate concept
    - Reduce MMP activity
    - Reduce inflammation to allow proliferation
    - Sparing of newly formed tissue, disrupt Cullens cycle
    - Promoted ACTIVE recruitment of Cells and active activation of physiology
- Ag addition as Antimicroial (takes Collagen Ag out of biologicals)
    - Ag also Anti MMP claim synergy
- Collagen ECM dressings
- Start bottom up synthesis
    - Increase addition of ECM components – GAGs, hyaluronic acid

Collagen Dressing Additives (current and potential)

ORC	Oxygenated Regenerated Cellulose	Absorb/release GFs, cytokines Absorb MMPS Improve flexibility Improve absorption Hemostasis
Alginate	Alginate	Improve absorption Improve gelling properties
Ag	Silver Numerous formulations	Antimicrobial Inactivate MMPs
EDTA	Ethylenediaminetetraacetic acid Glycosaminoglycans	Chelating agent Irreversibly inactivates MMPs
Glycerin	Sugar Alcohol	Humectant Lubricant
GAGs	Glycosaminoglycans	Improve Flexibility and conformability Absorb water / moisten Biochemical signaling Sequesters GFs, cytokines
CMC	Carboxymethyl cellulose	Absorption (like Aquacel) Conformability
Laminin	High MW proteins (3 chains alpha, beta Lambda) Glycoproteins	ECM component Molecular signals
Hyaluronic acids	Non-sulphated GAG	ECM component Signaling Support Moisture

Proteoglycans		
	Heavily Glycosylated Protein with GAG Small / Large	Structure Mediators Lubrication
Fibronectin		
	High MW Glycoprotein Soluble / Insoluble	Cell adhesion Growth, migration
GHK-Cu	Copper peptide	Proliferation/contraction

Next, “Top Down” processed animal tissue for collagen ECM Matix
(refer to Addendum #2: Collagen dressings currently on the market)

- Maintains ‘normal’ structure, dermal regeneration template
- Maintains normal GFs, cytokines within intact ECM (biomolecule resevoir)
- Resorbable, digested and replaced by healing tissue
- Not effective for managing exudate
    - Fenestrate
- Animal derived ECM (Endoform, Oasis, Matristem)
    - Other HCPCS surgical dressings and Q code CTPs
    - Line estensions, particles, flowables not autologous use – not covered.

During the early evolution of advanced wound care dressings, most efforts ended up being directed to the creation of a suite of products (film, hydrocolloid, hydrogel, foam, alginate, super absorber) dedicated to moderating the level of exudate presented at the wound/dressing interface.

Dressing materials were selected for their fluid absorption or release characteristics, followed by their ability to fill space and maintain intimate contact with the wound surface.

This consideration of the M (moisture) in TIME (wound bed preparation tool) followed the accepted principle that the wound fluid contained the essential cellular and biochemical ingredients at the appropriate place and time to maximize the healing potential of the wound.

The goal was to create and support an appropriate environment for the body to do its work, and to interfere with the normal healing process as infrequently as possible.

While a significant step forward from traditional wound care, the dressing action is passive. It provides a warm moist environment and the body does the rest.

While practical solutions to dressing wounds went on, the basis for wound chronicity were being explored and discussed in the quest to improve understanding and treatment of chronic wounds.

Dr. G. Sibbald introduced the TIME tool to insure each of the recognized barriers to chronic wound healing was examined and addressed serving as a guide to both wound treatment and product development.

Inflammation (the 'I' in the TIME tool) due to critical colonization or infection guarantees healing failure and may be addressed through the consideration of the NERDS and STONEES tools.

Aggressive removal of microbes encourages surgical and sharp debridement, wound cleansers with surfactants and antimicrobials/antiseptics.

Consideration of the infection issue was intimately responsible for the creation of the Antimicrobial dressings utilizing silver (the most widespread), PHMB (AMD gauze) and Honey.

Antimicrobial actives within these dressing created a new sub-category of dressings tracked as antimicrobial dressings, and listed as "Dressing, wound drug" for 510(k) registration purposes.

Collagen dressings containing silver fell into this classification, losing their identity as Biologicals.

Sources of chronic inflammation received more scrutiny and two factors were identified for intense discussion and study:

1. **Critical colonization** and the recent recognition of biofilm as an inflammatory stimulus
2. **MMPs** present in chronic wound fluid and their contribution to chronic inflammation (Cullen's Cycle)

1. Critical colonization influenced the development of wound dressings, and lead to the introduction of the numerous antimicrobial dressings.

The antimicrobial dressings were, for the most part, advanced (MWH) wound dressings to which antimicrobial agents were added. The most extensive example is the large number of dressings containing antimicrobial silver such as:

- Foam plus silver
- Alginate plus silver
- Film plus silver
- Hydrogel plus silver
- **Collagen** plus silver

Less expensive antimicrobial dressing lines include PHMB (AMD Dressing), and a great deal of the interest in Honey stems from claims of its antimicrobial (and thus anti-inflammatory) properties.

Beyond its influence on wound dressings, the role of critical colonization and biofilm in creating chronic wound has led to increased consideration and utilization of Iodine, wound cleansers, antiseptics and debriding agents (passive, pads and powered, Ultrasound, Hydrojet).

The colonization/biofilm research and discussion drive interest in specialized products and techniques, and consideration of the immune process and the generation of inflammatory mediators.

Diagnostic devices/products that can detect and quantify the presence of inflammatory mediators in the wound are being developed (e.g. WoundChek), with the promise of ensuring wounds with inflammation/infection problems can be singled out for more intense and focused treatment.

2. MMPs

MMPs (Matrix Metalloproteases) have received intense attention since it was determined that they appeared in higher concentrations and varieties in the chronic wound fluid.

Several studies have indicated that high and persisting MMP levels are characteristic of chronic wounds, and the roles several mechanisms explaining their relevance as barriers to healing have been proposed.

MMPs are involved in the digestion of collagen, and collagen breakdown products are implicated in both normal and abnormal healing pathways.

In the chronic wound, high levels of MMPs and low levels of TIMPs are claimed to be responsible for maintaining the inflammatory state and for destruction of ECM as fast as it can be produced by fibroblasts.

MMP reduction is associated with:

- Reduction of infection/colonization/biofilm
- Use of Collagen Dressings as a sacrificial substrate to spare newly formed ECM.

Methods to reduce the presence of MMPs in the wound include:

- Removal of devitalized tissue (necrosis, slough) that stimulates MMP release
    - Debridement, cleansing
- Removal of microbial/ immune stimulation of enzyme release
- Absorption of MMPs into absorptive dressings
    - Sequester MMPs in foam dressing, alginate dressing or superabsorber
- Removals of exudate associated MMPs through VAC/NPWT
- Provision of sacrificial substrate-Collagen Dressings

Summary: Collagen dressings and MMPs

A key component identified in chronic wound is an elevated and persistent level of MMPs. At elevated levels, MMPs degrade damaged ECM and non-viable tissue and viable collagen otherwise destined to fill in the deficit.

Fibroblasts in chronic wounds fail to secrete sufficient TIMPs to maintain a positive replacement rate, and these events result in an inhibition of the deposition of the ECM/granulation tissue required for normal cell migration, and the coordination of wound repair in 3-dimensions.

Collagen dressings have been recommended as a means of reducing MMP effects on wound healing by serving as a sacrificial substrate to effectively divert some of the MMP activity away from newly-forming ECM (collagen sparing)

Scaffolding

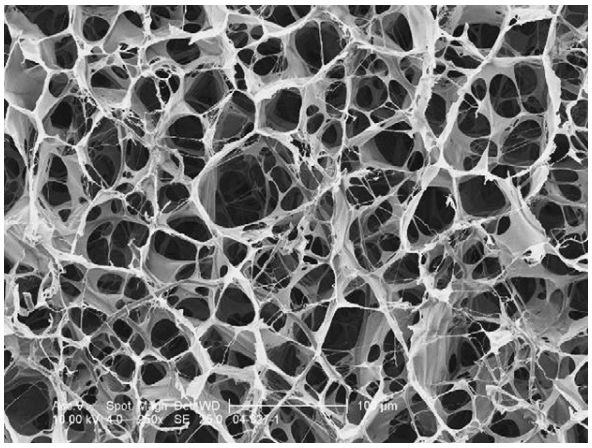
All wounds involve damage to the ECM and associated tissue. Chronic wounds often present as craters with significant absence of tissue which must be replaced.

Traditional and advanced wound care dressings provide an appropriate environment for the generation of granulation tissue on epithelium to fill and seal the wound; however, the granulation process takes time and resources (nutrients) to assemble the replacement tissue.

One benefit of the NPWT approach is that the negative pressure improves on normal wound contraction, reducing the amount of material that must be produced to fill the wound (shortens healing time).

An alternative approach to reducing granulation tissue requirements is to provide a 3-dimensional scaffold that takes the healing process from 2-dimensions, building layer-upon-layer, to repopulate the 3-dimensional scaffold.

Early approaches to this scenario were characterized by the creation of simple collagen sponges from various natural sources.



The structural details of the scaffold can be varied during the (bottom up) production of the dressing to define crosslinking, pore size, and additives. The treatment of animal or human tissue to remove cells (top down) strives to maintain natural tissue matrix structure to more closely resemble the tissue to be replaced. Addendum #1 lists Collagen dressings and their marketing descriptions. Addendum #2 provides a comprehensive review of available collagen dressings and their properties.

Regulatory

In Europe, ECM Collagen products fall under Class III regulations which are considerably more stringent and restrictive that the 510(k) premarket notification required in the USA.

In the USA, Collagen/ECM matrix products are now reviewed as *"Dressing, Wound Collagen," "Dressing Wound Drug"* (Ag products), or come to market through CYBER as 21 CFR 1271 products regulated under PSA section 361 as "minimally manipulated *Cellular and Tissue Derived Products* (CTPs of animal or human origin)."

Early 510(k) notifications for collagen began with soluble collagens used for platelet aggregation (in vitro,) followed by its use in eye shields.

Micro-collagen Pharmaceuticals introduced a Collagen Dermal wound spray (k920642) under *"Dressing, wound and burn, HYDROGEL W/Drug and/or biologic".*

Sween introduced their collagen product in 1993 (K926389), using CYBER instead of CDRH.

Fibracol (K925548) was approved under Syringe, Piston and Heliderm Collagen wound dressing was approved (K990086) under device classification Dressing, Wound Drug.

The classification name *Dressing, Wound Collagen* appeared with the Adri Product Foam Topical Wound Dressing with Collagen (K000054/review code KGN).

Ferris Listed Polymem sterile wound dressing with collagen (K002129) under device classification under CYBER as *Dressing, Wound and Burn, Hydrogel with drug and/or biologic.*

Continuing the trend, Southwest Technologies introduced its Stimulen line of collagen dressing product (with SWT traditional glycerin) K030774 under *Dressing, Wound Collagen*.

While significantly more sophisticated and obviously a SIS ovine collagen membrane, OASIS (Oasis Research at the time) received its 510(k) under device classification name *Dressing, Wound Collagen (KGN),* clearing the way for higher level products to receive simple 510(k) clearances.

Most Collagen dressings after this time are filled under Classification *Dressing, Wound Collagen* or under CYBER PSA 361 (minimally processed tissue) to seek higher reimbursement potential.

It is interesting to note that some of the 510(k) collagen dressings sell as surgical supplies (dressings), and are reimbursed under HCPCS "A" codes at dressing rates, while others with 510K(k)s are reimbursed as Cellular and Tissue derived Products (CTPs) under the same Q Codes designations as Skin Substitutes.

While no dollars are associated with the Q-code products, they are used in skin replacement procedures where the Facility and QHP receive significant fees for the procedures *(see Appendix 3).*

Collagen Powders such as Innocoll Collagen Powder (K103648) or the Collafirm product (K120250) are now classified under *Dressing, wound collagen (KGN)*.

Collagen wound gels such as Hydrolyzed Collagen Wound gel with Silver (Hymed Group) fall into device classification name "*Dressing, Wound Drug*," due to their silver content trumping the collagen component.

While practically ALL collagen dressings marketed in the USA make substantial marketing and scientific claims, NONE of their 510(k) summaries refer to any activity beyond those of Advanced Wound Care products.

Examples of 510(k) Summary claims and Indications for use are:
Stimulen
Intended Use:

- Stimulen™ Collagen is indicated for the management of wounds including full and partial thickness wounds, pressure ulcers (stages I-IV), venous stasis ulcers, diabetic ulcers, partial thickness burns, acute wounds, abrasions, traumatic wounds healing by secondary intention, donor sites and other surface wounds.

Prisma ORC
Intended Use:

- The Collagen-ORC Antimicrobial Matrix is intended for the management of exuding wounds

ColActive (Covalon)
Indications for Use:

- ColActive™ Collagen Wound Dressing is indicated for the management of full and partial thickness wounds

The addition of Silver to become "antimicrobial" collagen dressings can shift the Device Classification Name to *Dressing, Wound Drug (FRO),* where the silver appears to trump the collagen for review group. The silver antimicrobial claim is limited to *forming a barrier to reduce contamination*, and no claims are made on reducing wound contamination.

The addition of "Absorbable" to the claims for collagen entered 510(K) approvals as exemplified by Collagen Wound Dressing (K112580):

- Collagen Wound Dressing (Absorbable Collagen Membrane) is a sterile, pliable porous and dense wound dressing made of **highly** purified collagen derived from porcine skin. It is cross-linked using I1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide (EDC) for the resistance to enzymatic degradation. Collagen Wound Dressing is completely absorbable and **highly** biocompatible.
- Collagen Wound Dressing is composed of porous sponge layer for the wound surface and dense film layer for protecting wound from outside.

Puracol (K1071552) Plus Ag Collagen MICROSCAFFOLD wound dressing (Medline) introduced the micro-scaffold concept in its name but not in its claims. It reaffirmed claims for use under compression dressings, and the ability to be layered (stacked) to fill cavities. The Ag component assured its device classification was under Dressing, Wound Drug (FRO).

The AMS Collagen Dermal Matrix was classified under "Mesh, Surgical, Non Synthetic, Urogynocological for Stress urinary incontinence."

ARCHITECT Px Extracellular Collagen Matrix (K140367), made by Harbour Tech, is classified as "Dressing Wound Collagen" but marketed as a CTP product

Up until 1991, the 510(k) notification summary letters from the FDA specifically included restrictions to claims allowed for Collagen dressings:

Summary Letter for Skin Temp 1991

SPECIFIC RESTRICTIONS

- May not be labelled for 3rd degree burns
- May not be labeled as having any accelerating effect on the rate of wound healing
- May not be labeled as a long term, permanent or NO-Change Dressing or as an artificial skin

By 2005 these restrictions were no longer cited in 510(k) notifications, and while such claims were not included in the 510(k) filings, they were evident in the marketing of the products.

Note Summary Letter for ColActive 2005

General Controls (not specific restrictions)

NO restriction on burns, accelerating, or resorption

Note Summary Letter for Skin Temp II 2012

General Controls (not specific restrictions))

NO restriction on burns, Accelerating, or NO Change

Addendum #4 provides a listing of 510(k) summaries for both collagen dressings and Antimicrobial dressings containing collagen.

Reimbursement

Collagen dressings are reimbursed under HCPCS (CPT Level II) codes and, for some of the ECM products falling under 361 h/CTP, the Q codes.

HCPCS Surgical Dressing codes for collagen dressings fall into 3 groups, depending on the format (sheet, Powder/Particle or gel), as follows:

Dry Fillers

Collagen Based Wound Filler, dry form, sterile, per gram of collagen

HCPCS code A6010, $34.38 per gram

Examples of these products include:

- CellerateRx
- Helix-3CP
- Medifil Particles
- MPM triple helix collagen powder
- Stimulen Powder

Gel/Paste Fillers

Collagen Based Wound Filler, Gel/Paste, per gram of collagen

HCPCS Code A6011 $2.53

Examples of these products include:

- CellerateRx gel
- SilvaKollagen Gel
- Stimulen Collagen Gel

Sheet / Pad products

Collagen Dressing, Sterile size 16 square inches or less, each

HCPCs code A6021 $23.33

Examples of these products include:

Biostep/Biostep Ag	Lyophilized
ColActive/ColActive Ag	Lyophilized
Dermacol/Dermacol Ag	Lyophilized
Fibracol	Collagen Alginate
Promogran	
Prisma	
Puracol/Puracol Ag	
Endoform Dermal Template	(ECM from processed ovine stomach)

Collagen Dressing, Sterile size more than 16 square inches but less than 48 square inches, each

HCPCs code A6022 $23.33

Examples of these products include:

Biostep/Biostep Ag	Lyophilized
ColActive/ColActive Ag	Lyophilized
Dermacol/Dermacol Ag	Lyophilized
Fibracol	Collagen Alginate
Promogran	
Prisma	
Puracol/Puracol Ag	
Endoform Dermal Template	(ECM from processed ovine stomach)

Collagen Dressing, Sterile size more than 16 square inches but less than 48 square inches, each

HCPCs code A6023 $211.23

Examples of these products include:

- Colactive Plus Ag collagen matrix dressing 7” x 7”
- Helix-3 8” x 12”
- MPM Triple Helix 7” x 7”
- Puracol Ag Microscaffold
- SkinTemp II 8” x 12”

Rope/Ribbon format wound packing

Collagen Dressing, Wound Filler Sterile per 6 inches

HCPCs code A6024 $6.87

Examples of these products include:

- Fibracol Collagen-Alginate wound dressing

Collagen products containing Silver or other components providing improved performance are reimbursed at exactly the same rate as ‘plain,’ low-cost collagen products.

Third-party billers have no motivation to carry the higher-cost products, and will continue to seek lower cost items for the lines.

Hospitals and all other facilities are not reimbursed for their ‘supplies,’ such as dressings, and receive a fixed payment for the management of the patient from start to conclusion. Products that are more expensive that others (collagen dressings vs. alginates) may be selected when the case is made that overall treatment costs are reduced.

The A6022 code shows a reimbursement rate exactly the same as A6021 ($23.33).

There are many examples of this type of price duplication within the master HCPCS coding lists, and no reasonable explanation as to why the larger and smaller codes are reimbursed at the same rate.

Third-party billers already seeking to sell the smallest possible size product in A6021 are less than enthusiastic to supply the larger and more costly A6022 products, where their margins are further reduced.

Reimbursement levels for collagen products discourages innovation and limits the number of companies providing gel and filler products.

Most sales are in the 2" x 2" size where purchase cost is low and reimbursement is equal to that of much larger sizes. A surprising number of companies offer the infrequently used >48 inch formats; however, reimbursement is so high for this size range that revenues can be appreciable.

Collagen wound dressings were introduced as absorbers for exuding wounds, and the utilization guidelines (allowable) supports claim of one dressing per day.

The disconnect between the scaffolding (science) story and the daily dressing change (business) story seems to go unnoticed to this point.

For a complete listing of qualified Collagen dressings and their HCPCs codes see *Appendix 5*.

Cellular and Tissue derived Products Non-viable cells tissue abased animal source

The next group of collagen products include those derived from processing animal tissue in such a manner as to preserve some degree of dermal structure.

These products are promoted as scaffolding to guide the ingress, interaction and function of normal cells, and may be resorbed by the body, negating the need for frequent dressing changes.

These products are derived from animal tissue and include:

Endoform	Sheep stomach	Sold as Surgical Dressing
OASIS	Pig intestinal submucosa	Sold as Low Cost Skin substitute
Matristem Micromatrix	Lyophilized ECM particles	NO code
Matristem Multilayer matrix sheet		Sold as low cost Skin substitute
Architect Stabilized Collagen Matrix		Sold as low cost Skin substitute
Keramatix	Keratin/no collage	Sold as low cost Skin substitute
Integra	Collagen-Glucosaminoglycan	Sold as high cost Skin substitute

These products can be reviewed within the collagen category as their largest component is collagen. They are promoted as extracellular matrix products and may contain some or all of the components found in the extracellular matrix such as:

Proteoglycans
Non proteoglycan polysaccharides (Hyaluronic acid)
Fibers Collagen, elastin
Fibronectin, Laminin

With minimal processing, these products may provide a regenerative dermal template that is left in place to be resorbed while being replaced with the patient's own tissue. Those products marketed under Q codes, as Cellular and Tissue derived products (CTPs), **receive no reimbursement** for themselves as product. QHPs and Facilities using the products receive a **fee for the procedure** of applying a skin substitute.

Cellular and Tissue derived Products Non-viable cells tissue based human source (h/CTP)

To be inclusive, there is an addition group of products to be considered when seeking high level properties and activities related to collagen.

Several products with arguably high collagen content are produced through chemical treatment processes that remove all viable cells from human dermal or amniotic tissue.

These minimally-processed human tissues are regulated under CYBER and marketed as ECM dressings, regenerative matrix, or template products.

It is suggested that the natural structure and composition of these products provides biochemical and physical signals that guide the ingress, interaction and function of normal cells to repopulate the matrix, and may be resorbed by the body, negating the need for frequent dressing changes. Many suggest a single application may lead to complete healing.

H/CTP products:

Alloskin RT	Human meshed dermal allograft (ECM, GAGs, Cytokines)	Low Cost Skin substitute

CMS (Centers for Medicare Services) has created a two-tier reimbursement model that differentiated between CTPs, based on the price charged for the product.

Applying a low-cost CTP (less than $25.00 per cm2) qualifies for payment in the range of $400.00, while applying a high-cost CTP qualifies for a payment in the $1400.00 range (minus 20% copay).

The product cost is bundled in the procedure cost.

2015 HOPPS APCs for Skin Grating Procedures with High-Cost CTPs
Less than 100 SQ CM

CPT	Description	APC Category	APC	Fee 2015
15271	Skin sub graft trunk/arm/leg	Level III Skin Procedures	0328	$1,408.02
15272	Skin sub graft t/a/l add-on	included		
15275	Skin sub graft face/neck/ head/foot/groin	Level III Skin Procedures	0328	$1,408.02
15276	Skin sub graft f/n/hf/g addl	included		

2015 HOPPS APCs for Skin Grating Procedures with Low-Cost CTPs
Less than 100 SQ CM

C5271	Skin sub graft trunk/arm/leg	Level III Skin Procedures	0327	$430.89
C5272	Skin sub graft t/a/l add-on	included		
C5275	Skin sub graft face/neck/ head/foot/groin	Level III Skin Procedures	0327	$430.89
C5276	Skin sub graft f/n/hf/g addl	included		

2015 HOPPS APCs for Skin Grating Procedures with High-Cost CTPs
More than 100 SQ CM

CPT	Description	APC Category	APC	Fee 2015
15273	Skin sub graft trunk/arm/leg	Level III Skin Procedures	0328	$2,301.54
15274	Skin sub graft t/a/l add-on	included		
15277	Skin sub graft face/neck/ head/foot/groin	Level III Skin Procedures	0328	$1,408.02
15278	Skin sub graft f/n/hf/g addl	included		

2015 HOPPS APCs for Skin Grating Procedures with Low-Cost CTPs
More than 100 SQ CM

C5273	Skin sub graft trunk/arm/leg	Level III Skin Procedures	0327	$1,407.42
C5274	Skin sub graft t/a/l add-on	included		
C5277	Skin sub graft face/neck/ head/foot/groin	Level III Skin Procedures	0327	$430.89
C5278	Skin sub graft f/n/hf/g addl	included		

Market for Collagen Dressings

Collagen dressings are considered outside the traditional and advanced wound care markets (synthetic), and are reported within the Biological Wound Dressing Market segment.

GLOBAL MARKET REVENUES FOR ADVANCED DRESSING TECHNOLOGIES, THROUGH 2018
($ MILLIONS)

Segment	2011	2012	2013	2018	CAGR% 2013-2018
Synthetic wound dressings	2,633	2,678	2,824	3,336	3.4
Biological wound dressings	978	1,028	1,079	1,274	3.4
Natural wound dressings	782	830	900	1,380	8.9
Total	4,393	4,536	4,803	5,990	4.5

Biological Wound Dressings include:

- Tissue-Engineered Skin Substitutes
- Collagen
- Growth Factors

There is some overlap between the high-end collagen products and the low-end tissue engineered skin substitutes of both animal and human sources that needs to be taken into account when reviewing Collagen in wound healing.

Collagen products have evolved through bottom up constructed collagen dressings and top down processed animal or human tissue.

Lyophilized reconstructed sheets/pads, powders, gels **(reconstructed Bottom Up)**
Collagen with additions

Silver	Multiple
ORC	Promogran
Alginate	Fibracol
CMC	DermaCol
EDTA	Multiple
GAG	Multiple
Resorbable product	Multiple

Minimal modification of biological membranes/tissue (Top Down)

Animal derived:

Endoform, Oasis, MatriStem

Human derived:

Dermis	DermaPure (dCell)
Amnion	Epifix

The Biological Technologies market will evolve to contain more products that include more of the qualities of each subsection, leading to products achieving high-function from advanced reconstruction (more sophisticated bottom up products), and a wider array of new processes for animal tissue derived products.

Low-end will evolve higher claims / High-end will max claims – close the gap.

GLOBAL MARKET REVENUES FOR BIOLOGICAL TECHNOLOGIES
($ MILLIONS)

Segment	2011	2012	2013	2018	CAGR% 2013-2018
Artificial skin and skin replacement	508	551	585	655	2.3
Collagen products	370	375	394	508	5.2
Growth factors	100	102	100	111	2.1
Total	978	1,028	1,079	1,274	3.4

USA MARKET REVENUES FOR BIOLOGICAL TECHNOLOGIES
($ MILLIONS)

Segment	2011	2012	2013	2018	CAGR% 2013-2018
Artificial skin and skin replacement	304.8	330.6	351.0	393.0	2.3
Collagen products	166.5	168.8	177.3	228.6	5.2
Growth factors	70.0	71.4	70.0	77.7	2.1
Total	541.3	570.8	598.3	699.3	3.4

USA MARKET REVENUES FOR COLLAGEN
($ MILLIONS)

Segment	2011	2012	2013	2018	CAGR% 2013-2018
Dry formats	30.8	32.1	34.6	45.7	6.8
Collagen Sheets/Pads	124.9	125.7	131.	166.9	4.95
Collagen Gel	10.8	11.0	11.5	16.0	6.7
Total	166.5	168.8	177.3	228.6	5.2

While collagen products may have applications in the acute care market (hemostasis, wound dressings), the chronic wound applications dominate sales. Over 80% of Collagen dressing revenue is derived from the chronic wound segment.

While considerable interest and research is devoted to the development of skin substitutes and growth factors, the collagen products have considerable traction in the biological segment.

GFs and CTPs remain high-cost items with relatively low reimbursement. CTP competition is now a significant factor, and barriers to entry are expected to increase with increased demand for clinical studies required to gain local CMS coverage (LCD).

Cost of CTP production should fall with newer automated process providing some room for profit growth. On the other hand, CMS has effectively placed the brakes on growth for the upper end products by declaring them "HIGH COST" for reimbursement.

Growth factors have a long way to go before proving themselves as effective modalities in wound care, and cost of production is expected to remain high for several years.

Collagen dressings, on the other hand, are relatively well-reimbursed, and low-cost formats are readily available for third-party billers to generate both attractive profit margins and high monthly unit sales (allowable = 30 dressings per month.).

Companies continue to promote high science-based explanations and claims to support use of collagen dressings, and they can be expected to grow significantly over the next 5 years.

The major Wound Care marketing organizations are all invested in providing Collagen products, and may have both low-level and high-level products within their line.

Examples:

S+N	Biostep, Biostep Ag, Oasis
Acelity (KCI, Systagenix)	Prisma, Promogran, Fibracol, Graftjacket
Hollister	Endoform (high-end positioned at low-end price point)
Medline	Puracol, Puracol Plus Ag

Systagenix (now Acelity) was the first significant company in the sector, grabbed a significant market share, and has managed to keep it in the face of competition with known products, aggressive marketing (claims), and the ability to bundle its offerings with all major GPOs and distributors.

Its acquisition by KCI adds the top CTP product to the line providing high- and low-end market offerings.

Medline wields power as one of the largest distributors with its own brands of collagen products (Puracol), and actively promotes Native Collagen vs denatured (gelatin) products.

Smith and Nephew has had on-again, off-again success with its collagens (second generation Covalon products), and derives success more from its GPO/bundling position than from product differentiation.

Most wound care companies (small and large) now have some form of collagen offering, and their participation indicates that (despite high-level scientific debate of positioning) the market is open to any and all types of collagen dressing:

- Native / denatured / activated
- Antimicrobial
- Sheet, pad, dry, gel
- Plain, complex (with GAGs, Hyalurate or Glycerin)

There is still opportunity to create a product that can be marketed as the 'Ideal' Collagen Dressing; however, it is more likely that a science-based line of differentiated collagen products targeting specific wound conditions and healing objectives could be justified.

Such a line would invoke differing claims for different wound healing stages for example:

- High gelatin (denatured/activated) for early inflammatory stage activation
- Low Gelatin / high GAG matrix for proliferation stage (make pre-remodeling claims).
- Hydro Conductive (high pass through rate) for exuding inflammatory wounds (bio filtration) for highly exuding wounds (intense inflammation)
- Highly-organized structural matrix (resorbable) for high cosmetic and functional result (low remodeling)

New production processes now produce resorbable collagen 'thread' that can be processed like any other textile product (CollaFix MiMedx).

Such technology could lead to knit, woven or non-woven collagen sheet or pad products tailored to perform traditional or new functions.

Imagine knit collagen elastin sponges embedded in ECM gels containing all the right biologicals in all the right places in all the right concentrations (high-end), or woven or non-woven collagen 'gauze' to meet the needs for low cost third-party biller products.

The futuristic alternative to collagen threads/fabrics would be dressings' custom-created utilizing 3D print technology, with an ever expanding bank of "inks" generating custom-designed scaffolds seeded with appropriate GFs, Cytokines and potentially, stem cells.

Market Pricing *(see Appendix 6)*

While reimbursement for collagen dressings is relatively high ($23.00/$7.30 for 2” x 2” Hydrocolloid), manufacturers have given in to third-party biller demands and provide OEM and branded collagen dressings at extremely low pricing.

Foreign manufactures will deliver low-end weight and quality 2” x 2” dressings below $2.00, and high-quality Chinese producers will OEM 2” x 2” product for $2.87 at 100,000 unit volumes ($3.87/25,000 - $3.15/50,000).

Private label (Medline, MPM) or branded product can be purchased direct from distributors for:

		Low price	Moderate	High price
2x2				
	Plain	4.44	6.17	16.53
	With Silver	5.14	9.98	
	C+Alginate		7.20	
	C+Orc		12.98	
4x4				
	Plain	9.82	21.97	42.04
	With Silver	21.97	31.29	
	C+Alginate		16.83	
	C+Orc		48.08	
Amnion 2x2			3,100.00	

GPO pricing ranges at 35% to 50% below distributor direct.

Dry format Collagens are available from distributors at

	Medifil	gm	8.31
	Stimulen	gm	18.12
Gel formats			
	Stimulen	gm	2.32
	Woundress	gm	8.02

Summary

As a well-established segment of the biologicals market, Collagen products will continue to benefit from high expectations for improved wound healing.

The traditional dressing market is well into the commodity stage of development, and the Advanced Wound Care market is characterized by full-line providers with products in each of the advanced wound dressing niches.

While the low-end Collagen products have depressed the overall profit potential of the segment, there is interest and opportunity for science- and performance-based differentiation to guide product selection in those segments where DRG fee caps justify use of higher-cost products that reduce the total cost and duration of treatment.

There remains plenty of opportunity to differentiate between collagen offerings, both between competitors and within a specialized line providing niche products, with purpose-designed outcomes based on the changing needs of the healing wound.

Growth can be expected in all formats of collagen dressings, including DTY formats, dressings and gels. Tissue-derived collagen ECM offerings also offer opportunities to improve wound healing and generate revenue.

Appendix 1

Collagen Dressings (bioactive)

Appendix 1

Collagen Dressings (bioactive)

Collagen wound dressings are available as gels, pads, particles, pastes, powders, sheets or solutions derived from bovine, porcine, equine, ovine, piscine or avian sources. Collagen wound dressings are indicated for partial- and full-thickness pressure ulcers, diabetic ulcers, venous ulcers, donor sites, vascular ulcers, second-degree burns, abrasions, surgical wounds, and traumatic wounds.

Endoform Dermal Template™
Hollister Incorporated - Wound Care
Endoform Dermal Template™ has the strength of a dermal template with the simplicity of a collagen. Endoform contains 90% collagen and 10% intact native ECM.

Helix3™ Bioactive Collagen
Amerx Health Care Corp.
Helix3™ Bioactive Collagen is 100% type I bovine non-hydrolyzed collagen in matrix or particle form bovine collagen. Provides moist healing of draining wounds and absorbs excess wound fluids. Available in matrix dressing and powder forms.

Stimulen™ Collagen Powder
Southwest Technologies, Inc.
Stimulen™ Collagen Powder is composed of modified bovine collagens. When sprinkled in the wound, it dissolves to form a protective gel.

BIOPAD™
Angelini Pharma Inc.
BIOPAD™ is a 100% pure native equine type I collagen dressing.
Thicker dressing construction, containing five times the standard amount of collagen

BIOSTEP* Ag Collagen Matrix Dressing with Silver
Smith & Nephew, Inc.
BIOSTEP* Ag Collagen Matrix Dressing with Silver targets and deactivates excess MMPs to optimize wound closure for chronic wounds. Highly conformable and easy to apply. Unique dual-action MMP targeting & deactivation

BIOSTEP* Collagen Matrix
Smith & Nephew, Inc.
BIOSTEP* Collagen Matrix targets and deactivates excess MMPs to optimize wound closure for chronic wounds. Highly conformable and easy to apply. Unique dual-action MMP targeting & deactivation

Catrix® Wound Dressing
Lescarden Inc/Catrix®
Catrix® Wound Dressing is a micronized biodegradable cartilage powder indicated for the management of pressure, venous insufficiency and diabetic ulcers, burns, surgical incisions and radiation dermatitis.

CellerateRX® Gel
Wound Care Innovations, LLC
CellerateRX® Gel is a patented hydrolyzed collagen wound dressing (approximately 65% type I collagen). Appropriate for light to moderately exudative wounds.

CellerateRX® Powder
Wound Care Innovations, LLC
CellerateRX® Powder is a patented hydrolyzed collagen wound dressing (approximately 95% type I collagen). Appropriate for moderate to heavily exudative wounds. Absorbs up to 30 times its weight in exudate.

ColActive® Plus
Covalon Technologies, Ltd.
ColActive® Plus is a protease modulating matrix comprised of collagen, EDTA, alginate and CMC, indicated for the management of full- and partial-thickness wounds. EDTA permanently deactivates MMPs

CollaSorb® Collagen Dressing
HARTMANN USA, Inc.
CollaSorb® is a latex-free collagen wound dressing ideal for managing acute and chronic wounds. Composed of 90% pure collagen, 10% calcium alginate

DermaCol™ Collagen Matrix Dressing
DermaRite Industries, LLC
DermaCol™ Collagen Matrix Dressing is bioactive with dual MMP inhibition (collagen and EDTA) supports optimal moisture balance (CMC and alginate) and wound healing

Excellagen®

Appendix 1

Taxus Cardium Pharmaceuticals
Excellagen® is a highly refined fibrallar bovine Type 1 collagen topical gel (2.6%) designed to support favorable wound care management.

FIBRACOL® Plus Collagen Wound Dressing with Alginate
Systagenix - An Acelity Company
FIBRACOL® Plus combines the structural support of collagen with the exudate management of alginate. 90% collagen and 10% alginate. Structural support of collagen with the exudate management of alginate

Gentell Collagen [41]
Gentell Wound and Skin Care [42]
Gentell Collagen is a primary dressing for chronic non-healing wounds, wounds with minimal to heavy exudate, partial- or full-thickness, granulating or necrotic wounds, or second-degree burns.

Helicoll™
MCT Medical Solutions LLC
Helicoll™ is a reconstituted Type-I collagen sheet free of contaminants such as lipids, elastin and other immunogenic proteins. Transparent and dry membrane with flexibility and moderate tackiness. Bovine Type-I Collagen

Medifill™ II Particles
Human BioSciences, Inc.
Medifill™ II Particles consist of 100% bovine, native collagen prepared with Kollagen™ technology. Absorbs 40-60 times its weight. Type 1 bovine collagen Powder/flake form.

PROMOGRAN PRISMA® Matrix
Systagenix - An Acelity Company
PROMOGRAN PRISMA® Matrix is comprised of 44% oxidized regenerated cellulose (ORC), 55% collagen and 1% silver-ORC in a sterile, freeze-dried composite.

PROMOGRAN® Matrix
Systagenix - An Acelity Company
PROMOGRAN® Matrix is comprised of 45% oxidized regenerated cellulose (ORC) and 55% collagen in a sterile, freeze-dried composite.

Puracol® Plus MicroScaffold™ Collagen
Medline Industries, Inc.
Puracol® Plus MicroScaffold™ Collagen is a native collagen wound dressing with a unique three-dimensional Microscaffold™ that promotes natural healing. Pure bovine-derived collagen in its native triple-helix formatAlso available in rope version.

Simpurity™ Collagen Pad
Safe n' Simple
Simpurity™ Collagen Pad is a unique porous 100% collagen dressing for moist wound healing environments. 100% non-bleached, native undigested bovine collagen

Simpurity™ Collagen Powder
Safe n' Simple
Simpurity™ Collagen Powder is a unique porous 100% collagen powder for moist wound healing environments

SkinTemp™ II Dressings
Human BioSciences, Inc.
SkinTemp™ II Dressings are 100% native collagen in non-hydrolyzed form. Type 1 bovine collagen

Stimulen™ Collagen Gel
Southwest Technologies, Inc.
Stimulen™ Collagen Gel is a concentrated dispersion of modified collagens already in amino acid form. Provides a highly concentrated dispersion of modified collagen. Used to fill wound cavity.

Stimulen™ Collagen Lotion
Southwest Technologies, Inc.
Stimulen™ Collagen Lotion is a liquid that forms a gel. Fluidizes immediately with agitation. Composed of modified collagens and glycerine. Fluidizes immediately with agitation or when applied to the skin. Moisturizes and conditions the skin.

Stimulen™ Collagen Sheets
Southwest Technologies, Inc.
Stimulen™ Collagen Sheets are composed of modified collagens and glycerine. Can be cut to size of wound cavity. Soluble on interaction with wound exudate.

Triple Helix Collagen Dressing
MPM Medical, Inc.
Triple Helix Collagen Dressings contain 100% type I collagen for use on partial- and full-thickness wounds.

Appendix 2

Collagen Competitive Products

Appendix 2:

Collagen Competitive Products

Product	BIOSTEP™ Collagen Matrix	BIOSTEP™ Ag Collagen Matrix Dressing with Silver	FIBRACOL* Plus Collagen Wound Dressing w/ Alginate	PROMOGRAN PRISMA* Matrix AG	PROMOGRAN* Matrix	Puricol	Puracol® Plus Microscaffold	Puracol® Plus Ag MicroScaffold ™ Collagen
Company	**Smith & Nephew, Inc.**	**Smith & Nephew, Inc.**	**Systagenix Wound Management**	**Systagenix Wound Management**	**Systagenix Wound Management**	**Medline Industries, Inc.**	**Medline Industries, Inc.**	**Medline Industries, Inc.**
Features	Porcine Type-1 plus denatured plus EDTA	Porcine Type-1 plus denatured plus EDTA + Ag	90% collagen 10%alginate	44% ORC 55% collagen 1% A ORC	45% ORC 55% collagen	100% collagen High Nativity	native collagen bovine triple helix	native collagen bovine triple helix
Gels on contact w/ exudate	x	x	x	x	x	x	x	x
Secondary dressing required	x	x	x	x	x		x	x
Usable on infected wounds				x		x		
Low adhesion	x	x	x	x	x	x	x	x
Conforms readily to wound	x	x	x	x	x	x	x	x
Moldable	x	x	x	x		x	x	x
Flexible	x	x	x	x	x	x	x	x
Cuttable	x	x	x	x	x	x	x	x
Variety of sizes	2	2				3		
Compatible w/ topicals	x	x	x	x	x	x	x	x
Combination product	x	x	x	x	x		x	x
powder available								
Does not require removal						x		
Contains silver		x		x				x
OTHER	high absorption	high absorption		frezze dried composite	frezze dried composite		microscaffold	
HCPCS Code	A6021	A6021	A6021, 22, 23 ,24	A6021 a6022	A6021, 22		A6021, 22, 23	A6021, 22
Sizes	2x2 4x4	2x2 4x4	2"x2", 4"x4.75" 4"48.75",rope '3/8"x 15.75"	4.34sq in 19.1 sq in	4.34sq in 19.1 sq in		2x2.25 4.25x4.25 8x8, rope 1"x8"	2'x2' 4'x4.5" rope
510(k)	Covalon	Covalon	K925548 K982597	K033523	K014129	K71552	A6021, 22, 23 A6024	K071552

Appendix 2:

Collagen Competitive Products

Product	CollaSorb® Collagen Dressing	BIOPAD	Triple Helix Coll Dressing	BGC Matrix®	DermaCol	ENDOFORM Dermal Template	MatriStem	Stimulen™ Collagen Sheets
Company	**HARTMANN USA, Inc.**	**Angelini**	**MPM**	**MoInlycke Brennen Medical, LLC**	**DermaRite Industries**	**Hollister**	**Acell**	**Southwest Technologies, Inc.**
Features	90% collagen 10% Ca Alginate bovine	100% Equine type I thicker	110% type-1 collagen	Beta	Collagen EDTA CMC Alginate	90% col. 10%ECM sheep ovine	Porcine Urinary Bladder	modified collagen and glycerine
Gels on contact w/ exudate	x		x	x	x		1 format	x
Secondary dressing required	x	x	x		x	x	x	x
Usable on infected wounds		x						x
Low adhesion		x	x				x	x
Conforms readily to wound	x	x	x	x	x		x	x
Moldable		x	x	x	x		x	x
Flexible	x	x	x	x	x		x	x
Cuttable	x	x	x	x			x	x
Variety of sizes			x		x	x		x
Compatible w/ topicals	x		x	x				x
Combination product	x			x				x
powder available								
Does not require removal							x	
Contains silver								
OTHER	30x absorb	5x standard collagen		Beta Glucan	EDTA	ECM	Decelularised	
HCPCS Code	A6201	A6021	A6010 A6021		A6021	A6021, 22	Q4119 Q4118 Q4119 Q4120	A6021, 22, 23
Sizes	2x2 4x4	2x2	2x2 rope 1oz packet		2x2 4x4	2"x2", 4"x5" Plain and fenestrated		2x3 4x4 6x8 12x12
510(k)	K091338	K040283				K092096	K112409 K092926	k030774

Appendix 2:

Collagen Competitive Products

Product	Stimulen™ Collagen Lotion	Stimulen™ Collagen Powder	Stimulen™ Collagen Gel	CellerateRx® Gel	CellerateRx® Powder	SkinTemp™ II Dressings	MediFill II Particles	Helix3 Bioactive Collagen
Company	**Southwest Technologies, Inc.**	**Southwest Technologies, Inc.**	**Southwest Technologies, Inc.**	**Wound Care Innovations, LLC**	**Wound Care Innovations, LLC**	**Human Biosciences**	**Human Biosciences**	**Amerx**
Features	Lotion-->gel collaen and glycerine	bovine	bovine	65% Type I filler	95% type-I	bovine type-I	100% bovine	100% Bovine type I
Gels on contact w/ exudate	x	x	x		x	x	x	x
Secondary dressing required							x	x
Usable on infected wounds				x		x	x	x
Low adhesion		x	x			x		
Conforms readily to wound	x	x	x	x	x	x	x	x
Moldable		x				x	x	x
Flexible	x	x	x		x	x	x	x
Cuttable	x	x	x	x	x	x	x	x
Variety of sizes						x		x
Compatible w/ topicals	x	x	x	x	x		x	x
Combination product	x	x		x	x			
powder available							x	x
Does not require removal			x	x	x			
Contains silver								
OTHER	modified collagen and glycerine			"Activated" Denatured Hydrolized	30x asoption		Powder/Flake 40-60 x absorb	
HCPCS Code		**A6010**	A6011	A6011	A6010	A6021 A6023	A6010	A6010, A6021, A6022
Sizes	2oz bottle 5 packet	**10g 20g, 40g 1gpch**	15 30g 5gpacket	6g 28g	1g 5g	2"x2", 3"x4", 8"x12". 5	1g, 5 vials per box.	1g, 2x2 3x4 4x5.23
510(k)					k122325 k925545 k91		K910944	

Appendix 2:

Collagen Competitive Products

Product	ColActive Plus	Excellagen	HeliColl	Simpurity Collagen Pad	Simpurity Collagen Powder	Gentell Collagen	Gentell Collagen with Ag	Gentell Collagen particles
Company	**Covalon Technologies, ltd**	**Taxus Cardium Pharmaceuticals**	**MCT Medical Solutions LLC**	**Safe n Simple**	**Safe n Simple**	**Gentell**	**Gentell**	**Gentell**
Features	Colagen EDTA Alginate & CMC	gene tech BOVINE TYPE-i	Bovine type-I reconsituted sheet	100% collagen bovine type-1	100% collagen bovine type-1	type-1	type-1	type-1
Gels on contact w/ exudate	x				x	x	x	x
Secondary dressing required	x	x		x	x	x	x	x
Usable on infected wounds	x	no		x	x			
Low adhesion								
Conforms readily to wound	x	x		x	x	x	x	x
Moldable	x			x	x	x	x	x
Flexible	x	x		x				
Cuttable	x			x		x	x	
Variety of sizes	x					x	x	
Compatible w/ topicals								
Combination product								
powder available					x			x
Does not require removal		x						
Contains silver								
OTHER	40x asorptionEDTA /MMPs		REQUIRES REHYDRATION					
HCPCS Code	A6021 A6022			A6021	A6010	A6021 A6022	A6021 A6022	A6010
Sizes	2x2 4x4 7x7	syringe flowable 0.5cc	25sq cm, 50sq cm, 100sq cm, 400sq cm	2x2	1g vial 1g packet	2 x2, 4 x 5.25	2 x2, 4.5"x4.5"	1gm 30/cs
510(k)	K043296 K050177	K110318						

Appendix 2:

Collagen Competitive Products

Product	Catrix Wound Dressing
Company	Lescarden Inc.
Features	bovine cartilage 50% micronized collagen
Gels on contact w/ exudate	
Secondary dressing required	x
Usable on infected wounds	x
Low adhesion	
Conforms readily to wound	x
Moldable	
Flexible	
Cuttable	
Variety of sizes	
Compatible w/ topicals	x
Combination product	
powder available	x
Does not require removal	x
Contains silver	
OTHER	10x absorption 73% proteib, 18 %Carbohydrates
HCPCS Code	A6262
Sizes	1g 14/bx
510(k)	CTP?

Appendix 3

2015 Reimbursement for CTPs

Appendix 3:

2015 Reimbursement for CTPs

2015 HOPPS APCs for Skin Grating Procedures with High-Cost CTPs
Less than 100 SQ CM

CPT	Description	APC Category	APC	Fee 2015
15271	Skin sub graft trunk/arm/leg	Level III Skin Procedures	0328	$ 1,408.02
15272	Skin sub graft t/a/l add-on	included		
15275	Skin sub graft face/neck/ head/foot/groin	Level III Skin Procedures	0328	$ 1,408.02
15276	Skin sub graft f/n/hf/g addl	included		

2015 HOPPS APCs for Skin Grating Procedures withl Low-Cost CTPs
Less than 100 SQ CM

C5271	Skin sub graft trunk/arm/leg	Level III Skin Procedures	0327	$ 430.89
C5272	Skin sub graft t/a/l add-on	included		
C5275	Skin sub graft face/neck/ head/foot/groin	Level III Skin Procedures	0327	$ 430.89
C5276	Skin sub graft f/n/hf/g addl	included		

2015 HOPPS APCs for Skin Grating Procedures with High-Cost CTPs
More than 100 SQ CM

CPT	Description	APC Category	APC	Fee 2015
15273	Skin sub graft trunk/arm/leg	Level III Skin Procedures	0328	$ 2,301.54
15274	Skin sub graft t/a/l add-on	included		
15277	Skin sub graft face/neck/ head/foot/groin	Level III Skin Procedures	0328	$ 1,408.02
15278	Skin sub graft f/n/hf/g addl	included		

2015 HOPPS APCs for Skin Grating Procedures withl Low-Cost CTPs
More than 100 SQ CM

C5273	Skin sub graft trunk/arm/leg	Level III Skin Procedures	0327	$ 1,407.42
C5274	Skin sub graft t/a/l add-on	included		
C5277	Skin sub graft face/neck/ head/foot/groin	Level III Skin Procedures	0327	$ 430.89
C5278	Skin sub graft f/n/hf/g addl	included		

Appendix 4

510(k) Premarket Approvals by Date

Appendix 4:

510(k) Premarket Approvals By Date

Dressing Wound Collage | Dressing Wound Collagen | KGN | Plastic and reconstructive surg.

PRODUCT	COMPANY	DECISION DATE	510(K) NUMBER
MEDEOR MATRIX WOUND DRESSING	KENSEY NASH CORPORATION DBA DSM	2/17/2015	K141738
Wound Matrix TF	MIROMATRIX MEDICAL INC.	1/27/2015	K143426
ARCHITECT PX EXTRACELLULAR COLLAGEN MATRIX	HARBOR MEDTECH INC.	9/12/2014	K140367
PREMVIA	BIOTIME INC.	8/7/2014	K134037
BIO-CONNEKT WOUND MATRIX	MLM BIOLOGICS INC.	7/22/2014	K140456
MIROMATRIX WOUND MATRIX	MIROMATRIX MEDICAL INC.	6/19/2014	K140510
MARIGEN WOUND DRESSING	KERECIS LIMITED	10/23/2013	K132343
COVAGEN	COVALON TECHNOLOGIES LTD.	8/16/2013	K123756
PRIMATRIX DERMAL REPAIR SCAFFOLD	TEI BIOSCIENCES INC.	8/5/2013	K131286
FIBRILLAR COLLAGEN WOUND DRESSING	COLLAFIRM LLC	4/21/2013	K120250
BRIDGE EXTRACELLULAR COLLEGEN MATRIX	HARBOR MEDTECH INC.	2/26/2013	K122502
SKINTEMP II	HUMAN BIOSCIENCES INC.	10/26/2012	K122325
PROCOLL	INNOCOLL PHARMACEUTICALS	6/21/2012	K120339
COLLAGEN WOUND DRESSING	DALIM TISSEN CO. LTD.	6/1/2012	K122115
PORCINE DERMAL XENOGRAFTS PORCINE DERMAL MATRIX	BRENNEN MEDICAL LLC	3/23/2012	K113866
MESO WOUND MATRIX	KENSEY NASH CORPORATION	2/10/2012	K112888
INTEGRA WOUND MATRIX (THIN)	INTEGRA LIFESCIENCES CORPORATION	2/9/2012	K113104
EXCELLAGEN	TISSUE REPAIR COMPANY	10/3/2011	K110318
COLLAGEN POWDER	INNOCOLL PHARMACEUTICALS LTD	9/14/2011	K103648
UNITE BIOMATRIX	SYNOVIS ORTHOPEDIC & WOUNDCARI	9/7/2011	K112399
MATRISTEM WOUND MATRIX	ACELL INC	8/29/2011	K112409
CORELEADER COLLA-PAD MODEL CS 03030	CORELEADER BIOTECH CO. LTD.	5/20/2011	K102946
SURGIAID	MAXIGEN BIOTECH INC.	2/2/2011	K100927
COLLEXA	INNOCOLL PHARMACEUTICALS	10/28/2010	K100574
ENDOFORM DENTAL TEMPLATE	MESYNTHES LTD	6/23/2010	K101546
COLLAGEN SPONGE	INNOCOLL PHARMACEUTICALS	2/16/2010	K092805
ENDOFORM DERMAL TEMPLATE	MESYNTHES LTD	1/21/2010	K092096
ACELL MATRISTEM WOUND SHEET	ACELL INC	10/28/2009	K092926

Appendix 4:

510(k) Premarket Approvals By Date

Dressing Wound Collage | Dressing Wound Collagen | KGN | Plastic and reconstructive surg.

PRODUCT	COMPANY	DECISION DATE	510(K) NUMBER
COLLASORB COLLAGEN WOUND DRESSING	HARTMANN-CONCO INC.	8/26/2009	K091338
THERAFORM STANDARD/SHEET	SEWON CELLONTECH CO. LTD.	7/30/2009	K090812
ATLAS WOUND MATRIX	WRIGHT MEDICAL TECHNOLOGY INC.	7/30/2009	K090954
AONGEN COLLAGEN MATRIX	AEON ASTRON EUROPE B.V.	5/14/2009	K080868
AWBAT-S AWBAT-D AWBAT-M	AUBREY INC.	2/6/2009	K082869
PRIMATRIX DERMAL REPAIR SCAFFOLD	TEI BIOSCIENCES INC.	12/12/2008	K083440
HYDROLYZED COLLAGEN WITH 10% CHONDROITIN SULFATE (P	APPLIED NUTRITIONALS	10/30/2008	K081724
LTM WOUND DRESSING	LIFECELL CORP.	10/8/2008	K082103
COLLIEVA	INNOCOLL PHARMACEUTICALS	9/30/2008	K081782
INTEGRA FLOWABLE WOUND MATRIX MODEL FWD301	INTEGRA LIFESCIENCES CORP.	10/10/2007	K072113
UNITE BIOMATRIX	PEGASUS BIOLOGICS INC.	6/20/2007	K071425
MODIFICATION TO COLLAWOUND DRESSING	COLLAMATRIX CO. INC.	3/2/2007	K070269
HEALADEX-P	HEALAGENICS INC.	2/16/2007	K063517
COLLAGUARD MODEL FCIAFCIBFCICAND FCID	INNOCOLL PHARMACEUTICALS	10/2/2006	K061746
DERMADAPT WOUND DRESSING	PEGASUS BIOLOGICS INC.	9/21/2006	K061494
OASIS WOUND MATRIX	COOK BIOTECH INC.	7/19/2006	K061711
COLLAWOUND DRESSING	COLLAMATRIX CO. INC.	7/5/2006	K061474
PRIMATRIX DERMAL REPAIR SCAFFOLD	TEI BIOSCIENCES INC.	6/29/2006	K061407
ACELL POWDER WOUND DRESSING	ACELL INC	6/23/2006	K060888
MEDLINE COLLAGEN WOUND DRESSING	MEDLINE INDUSTRIES INC.	6/19/2006	K060456
COLACTIVE COLLAGEN WOUND DRESSING	COVALON TECHNOLOGIES INC.	4/27/2005	K050177
HEALICOLL	ENCOLL CORP.	8/12/2004	K040314
STIMULEN COLLAGEN	SOUTHWEST TECHNOLOGIES INC.	8/9/2004	K030774
COLLAGEN WOUND DRESSING - ORAL	COLLAGEN MATRIX INC.	5/10/2004	K040403
MODIFICATION TO: COLLAGEN TOPICAL WOUND DRESSING	COLLAGEN MATRIX INC.	3/17/2004	K040558
MODIFICATION TO: COLLAGEN TOPICAL WOUND DRESSING	COLLAGEN MATRIX INC.	2/27/2004	K040211
DRESSSKIN	TEI BIOSCIENCES INC.	9/29/2003	K023778
COLLAGEN TOPICAL WOUND DRESSING	COLLAGEN MATRIX INC.	5/15/2003	K030921

Appendix 4:

510(k) Premarket Approvals By Date

Dressing Wound Collage | Dressing Wound Collagen | KGN | Plastic and reconstructive surg.

PRODUCT	COMPANY	DECISION DATE	510(K) NUMBER
ACELL UBM HYDRATED WOUND DRESSING	ACELL INC	12/30/2002	K022854
ACELL UBM LYOPHILIZED WOUND DRESSING	ACELL INC	12/19/2002	K021637
AVAGEN WOUND DRESSING	INTEGRA LIFESCIENCES CORP.	9/10/2002	K022127
SS MATRIX	COOK BIOTECH INC.	5/30/2002	K020732
COLLATEK POWDER	BIOCORE MEDICAL TECHNOLOGIES IN(	10/24/2001	K012990
FORTADERM WOUND DRESSING	ORGANOGENESIS INC.	6/13/2001	K011026
FOAM CALCIUM ALGINATE TOPICAL WOUND DRESSING	ADRI/TECHNAM	12/22/2000	K003134
COLLAGEN WOUND DRESSING	OASIS RESEARCH LLC.	10/18/2000	K002443
MEDTRADE PRODUCTS ALGINATE ISLAND	MEDTRADE PRODUCTS LTD.	4/18/2000	K000487
FOAM CALCIUM ALGINATE TOPICAL WOUND DRESSING WITH (	ADRI	3/13/2000	K000054
SIS WOUND DRESSING II	COOK BIOTECH INC.	1/6/2000	K993948
SIGNADRESS DUODERM DRESSING	CONVATEC A DIVISION OF E.R. SQUIBE	5/18/1999	K990964
HA ABSORBENT WOUND DRESSING	CONVATEC A DIVISION OF E.R. SQUIBE	3/3/1999	K984388
FIBRCOL PLUS COLLAGEN WOUND DRESSING WITH ALGINATE	JOHNSON & JOHNSON MEDICAL INC.	8/20/1998	K982597
SIS WOUND DRESSING	COOK BIOTECH INC.	4/30/1998	K973170
KENDALL HYDROPHILIC POWDER WOUND DRESSING	KENDALL HEALTHCARE PRODUCTS CO.	4/23/1997	K970266
HYCURE	THE HYMED GROUP CORP.	1/17/1996	K955506
MEDISKIN(R) SS ZENODERM BIOLOGICAL WOUND DRESSING	BRENNEN MEDICAL INC.	6/28/1995	K950032
MESH MATRIX WOUND DRESSING	BRENNEN MEDICAL INC.	4/13/1995	K950281
E-Z DERM BIOSYNTHETIC WOUND DRESSING	BRENNEN MEDICAL INC.	7/11/1994	K935189
SKINTEMP MODIFICATION	BIOCORE	2/23/1993	K925545
VIADERM	ABS LIFE SCIENCES	12/4/1991	K914024
SKINTEMP	BIOCORE	10/2/1991	K913023
COPOLYESTER FILM DRESSING	TRI-STATE HOSPITAL SUPPLY CORP.	10/16/1989	K893647
CUSTOM BURN DRESSING KIT	HERMITAGE HOSPITAL PRODUCTS INC	11/7/1984	K843788
BIOBRANE BRAND TEMPORARY WOUND DRESSING	WOODROOF LABORATORIES INC.	5/3/1979	K790496

Appendix 4:

510(k) Premarket Approvals By Date

Dressing Wound Collage

Dressing Wound Collagen

KGN

Plastic and reconstructive surg.

PRODUCT	COMPANY	DECISION DATE	510(K) NUMBER
ANTIMICROBIAL	**Dressing wound Drug**	**FRO**	
		Plastic and Reconstructive Surg.	
Collagran-Collagen wound dressing, colla	Covalon Technologies Ltd.	K060804	4/18/2006
Hydrolyzed Collagen/Ag Wound Gel with Silver	The Hymed Group Corp.	K132891	6/19/2014
Puracol Plus Ag Collagen Microscaffold with Silver	Medline Industries, Inc.	K071552	4/25/2008
Jydrolyzed Collagen/Ag wound gel with silver	The Hymed Group Corp.	K061227	12/20/2006
CovaClear Ag Collagen with Silver antimicrobial	Covalon Technologies Ltd.	K052696	2/3/2006
Colactive Ag Collagen with Silver antimicrobial	Covalon Technologies Ltd.	K043296	6/6/2005
Collagen-ORC Antimicrobial Matrix	Johnson & Johnson Medical, Ltd.	K033523	10/21/2004
Heliderm Collagen Wound Dressings 0.5 gr	Integra Lifesciences Corp.	K990086	3/31/1999

Appendix 5

DME PDAC Listings

Appendix 5:

DME PDAC Listings

A6010 — COLLAGEN BASED WOUND FILLER, DRY FORM, STERILE, PER GRAM OF COLLAGEN

Product Name	Manufacturer/Distributor	Model Number	HCPCS Code	Effective Begin Date
CELLERATERX	ADVANCED WOUND CARE INC		A6010 OR A6261	5/23/2002
CELLERATERX	WOUND CARE INNOVATIONS, LLC		A6010 OR A6011	6/4/2002
HELIX-3 CP	AMERX HEALTH CARE CORP	H40111	A6010	11/7/2014
MATRIX COLLAGEN PARTICLES	COLLAGEN MATRIX INC	MCP-10	A6010	8/28/2003
MEDIFIL PARTICLES	BIOCORE		A6010	1/1/2002
MEDIFIL II PARTICLES 1G	HUMAN BIOSCIENCES INC	MF 2001	A6010	5/17/2013
MPM TRIPLE HELIX COLLAGEN POWDER	MPM MEDICAL INC	MP00311	A6010	4/26/2013
NUMED COLLAGEN DRESSING	NUMED INDUSTRIES, LLC	NM50S0COL	A6010	2/1/2014
REPAIRRX (POWDER)	WOUND CARE INNOVATIONS, LLC		A6010	6/4/2002
SIMPURITY COLLAGEN	SAFE N SIMPLE LLC	SNS5001G	A6010	5/28/2014
SIMPURITY COLLAGEN PARTICLES	SAFE N SIMPLE LLC	SNS5221G	A6010	2/13/2015
STIMULEN COLLAGEN POWDER	SOUTHWEST TECHNOLOGIES INC	ST9501	A6010	2/16/2006
STIMULEN COLLAGEN POWDER	SOUTHWEST TECHNOLOGIES INC	ST9520	A6010	2/16/2006
STIMULEN COLLAGEN POWDER	SOUTHWEST TECHNOLOGIES INC	ST9540	A6010	2/16/2006
STIMULEN COLLAGEN POWDER	SOUTHWEST TECHNOLOGIES INC	ST9515	A6010	8/8/2009

A6011 — COLLAGEN BASED WOUND FILLER, GEL/PASTE, PER GRAM OF COLLAGEN

Product Name	Manufacturer/Distributor	Model Number	HCPCS Code	Effective Begin Date
CELLERATERX	WOUND CARE INNOVATIONS, LLC		A6010 or A6011	6/4/2002
SILVAKOLLAGEN GEL	DERMARITE INDUSTRIES LLC	500	A6011	5/15/2008
STIMULEN COLLAGEN GEL	SOUTHWEST TECHNOLOGIES INC	ST9502	A6011	11/24/2009
STIMULEN COLLAGEN GEL	SOUTHWEST TECHNOLOGIES INC	ST9503	A6011	11/24/2009
STIMULEN COLLAGEN GEL	SOUTHWEST TECHNOLOGIES INC	ST9504	A6011	11/24/2009
STIMULEN COLLAGEN GEL	SOUTHWEST TECHNOLOGIES INC	ST9506	A6011	11/24/2009

A6021 — COLLAGEN DRESSING, STERILE, EACH

Product Name	Manufacturer/Distributor	Model Number	HCPCS Code	Effective Begin Date
BGC MATRIX	BRENNEN MEDICAL		A6021-22-23	10/21/2003
BIOPAD EQUINE COLLAGEN	EURORESEARCH SRL	B220302	A6021	2/1/2007
BIOPAD EQUINE COLLAGEN 2X2 IN	EURORESEARCH SRL	B220302	A6021	6/6/2013
BIOSTEP AG	SMITH & NEPHEW INC	66800126	A6021	8/7/2013
BIOSTEP AG	SMITH & NEPHEW INC	66800122	A6021	8/7/2013
BIOSTEP AG C0LLAGEN MATRIX DRESSING	SMITH & NEPHEW INC	66800126	A6021	11/16/2007
BIOSTEP AG COLLAGEN MATRIX DRESSING	SMITH & NEPHEW INC	66800122	A6021	11/16/2007
BIOSTEP COLLAGEN MATRIX DESSSING	SMITH & NEPHEW INC	66800124	A6021	11/19/2007
BIOSTEP COLLAGEN MATRIX DRESSING	SMITH & NEPHEW INC	66800125	A6021	11/19/2007
BIOSTEP COLLAGEN MATRIX DRESSING	SMITH & NEPHEW INC	66800124	A6021	8/7/2013
BIOSTEP COLLAGEN MATRIX DRESSING	SMITH & NEPHEW INC	66800125	A6021	8/7/2013
COLACTIVE	HARTMANN-CONCO INC	49700000	A6021	10/17/2006
COLACTIVE	HARTMANN-CONCO INC	49710000	A6021	10/17/2006
COLACTIVE 90	COVALON TECHNOLOGIES INC	TWBC1048	A6021	5/3/2013
COLACTIVE 90	COVALON TECHNOLOGIES INC	TWBC1049	A6021	5/3/2013

Appendix 5:

DME PDAC Listings

COLACTIVE 90 AG	COVALON TECHNOLOGIES LTD	TWBC1051	A6021	4/26/2013
COLACTIVE 90 AG	COVALON TECHNOLOGIES LTD	TWBC1052	A6021	4/26/2013
COLACTIVE AG	HARTMANN-CONCO INC	49720000	A6021	10/17/2006
COLACTIVE AG	HARTMANN-CONCO INC	49730000	A6021	10/17/2006
COLACTIVE AG COLLAGEN WITH SILVER ANTIMICROBIAL DRESSING	COVALON TECHNOLOGIES LTD	CA00104	A6021	10/24/2006
COLACTIVE AG COLLAGEN WITH SILVER ANTIMICROBIAL DRESSING	COVALON TECHNOLOGIES LTD	CA00204	A6021	10/24/2006
COLACTIVE COLLAGEN WOUND DRESSING	COVALON TECHNOLOGIES LTD	CO00104	A6021	10/24/2006
COLACTIVE COLLAGEN WOUND DRESSING	COVALON TECHNOLOGIES LTD	CO00204	A6021	10/24/2006
COLACTIVE PLUS AG COLLAGEN MATRIX DRESSING WITH SILVER 2" X 2"	COVALON TECHNOLOGIES INC	TWBC1020 (30 DRESSINGS PER BOX)	A6021	4/26/2013
COLACTIVE PLUS AG COLLAGEN MATRIX DRESSING WITH SILVER 2" X 2"	COVALON TECHNOLOGIES INC	TWBC1033 (10 DRESSINGS PER BOX)	A6021	4/26/2013
COLACTIVE PLUS AG COLLAGEN MATRIX DRESSING WITH SILVER 4" X 4"	COVALON TECHNOLOGIES INC	TWBC1022 (30 DRESSINGS PER BOX)	A6021	4/26/2013
COLACTIVE PLUS AG COLLAGEN MATRIX DRESSING WITH SILVER 4" X 4"	COVALON TECHNOLOGIES INC	TWBC1034 (10 DRESSINGS PER BOX)	A6021	4/26/2013
COLACTIVE PLUS COLLAGEN MATRIX DRESSING 2" X 2"	COVALON TECHNOLOGIES INC	TWBC1016 (10 DRESSINGS PER BOX)	A6021	4/26/2013
COLACTIVE PLUS COLLAGEN MATRIX DRESSING 2" X 2"	COVALON TECHNOLOGIES INC	TWBC1017 (30 DRESSINGS PER POLYBAG)	A6021	4/26/2013
COLACTIVE PLUS COLLAGEN MATRIX DRESSING 4" X 4"	COVALON TECHNOLOGIES INC	TWBC1018 (10 DRESSINGS PER BOX)	A6021	4/26/2013
COLACTIVE PLUS COLLAGEN MATRIX DRESSING 4" X 4"	COVALON TECHNOLOGIES INC	TWBC1019 (15 DRESSINGS PER POLYBAG)	A6021	4/26/2013
COLACTIVE TRANSFER WOUND CONTACT LAYER 2 INCHES X 2 INCHES	COVALON TECHNOLOGIES INC	TWBT1040	A6021	3/6/2015
COLLASORB LATEX FREE COLLAGEN DRESSING	HARTMANN USA INC	49750000	A6021	3/12/2013
COLLASORB LATEX FREE COLLAGEN DRESSING	HARTMANN USA INC	49760000	A6021	3/12/2013
COLLIEVA BOVINE COLLAGEN MEMBRANE STERILE	COLLMED LABORATORIES	CV1.75-01	A6021	3/3/2008
COLLIEVA BOVINE COLLAGEN MEMBRANE STERILE	COLLMED LABORATORIES	CV3.5-01	A6021	3/3/2008
CORELEADER COLLA-PAD	CORELEADER BIOTECH COMPANY LTD	CS10100	A6021	6/6/2013
DERMACOL	DERMARITE INDUSTRIES LLC	00302E	A6021	6/6/2013
DERMACOL	DERMARITE INDUSTRIES LLC	00303E	A6021	6/6/2013
DERMACOL AG	DERMARITE INDUSTRIES LLC	00502E	A6021	6/6/2013
DERMACOL AG	DERMARITE INDUSTRIES LLC	00503E	A6021	6/6/2013
ENDOFORM DERMAL TEMPLATE	HOLLISTER INC	529311	A6021	1/1/2013
ENDOFORM DERMAL TEMPLATE	HOLLISTER INC	529312	A6021	1/1/2013
FIBRACOL COLLAGEN-ALGINATE WOUND DRESSING (COVER)	JOHNSON & JOHNSON (A DIVISION OF ETHICON INC)		A6021-22	1/31/2001
FIBRACOL PLUS COLLAGEN WOUND DRESSING WITH ALGINATE (COVER)	JOHNSON & JOHNSON (A DIVISION OF ETHICON INC)		A6021-22	1/31/2001
HELICOLL	ENCOLL CORP	HC2" X 4"	A6021	8/5/2013
HELICOLL	ENCOLL CORP	HC2" X 2"	A6021	8/5/2013
HELICOLL	ENCOLL CORP	HC4" X 4"	A6021	8/5/2013
HELICOLL COLLAGEN DRESSING	ENCOLL CORP	2" X 4"	A6021	2/15/2006
HELICOLL COLLAGEN DRESSING	ENCOLL CORP	4" X 4"	A6021	2/15/2006
HELICOLL COLLAGEN DRESSING	ENCOLL CORP	8" X 8"	A6023	2/15/2006
HELIX-3 CM 2" X 2" COLLAGEN MATRIX DRESSING (4 SQUARE INCHES)	AMERX HEALTH CARE CORP	H40221	A6021	12/30/2014
HELIX-3 CM 3" X 4" COLLAGEN MATRIX DRESSING (12 SQUARE INCHES)	AMERX HEALTH CARE CORP	H40222	A6021	12/30/2014
MATRIX COLLAGEN FILM	COLLAGEN MATRIX INC	MCF-2020	A6021	6/9/2004
MATRIX COLLAGEN FILM	COLLAGEN MATRIX INC	MCF-4040	A6021	6/9/2004

Appendix 5:

DME PDAC Listings

MATRIX COLLAGEN SPONGE WOUND DRESSINGS	COLLAGEN MATRIX INC	MCS-2030	A6021	3/23/2004
MATRIX COLLAGEN SPONGE WOUND DRESSINGS	COLLAGEN MATRIX INC	MCS-3040	A6021	3/23/2004
MEDIFIL PAD	BIOCORE		A6021	12/31/1999
MPM TRIPLE HELIX COLLAGEN DRESSING 2" X 2"	MPM MEDICAL INC	MP00310	A6021	4/26/2013
NUMED COLLAGEN DRESSING 4" X 4" SHEET	NUMED INDUSTRIES LLC	B-NM1010COL	A6021	4/24/2015
NUMED COLLAGEN PARTICLES	NUMED INDUSTRIES, LLC	NM10COL	A6021	2/1/2014
OASIS WOUND DRESSING DRY SHEET (FENESTRATED AND NON-FENESTRATED)	COOK BIOTECH INC		A6021-22	1/1/2003
PROMOGRAN MATRIX WOUND DRESSING 4.34 SQ INCH HEXAGON	SYSTAGENIX WOUND MANAGEMENT (US) INC	PG004	A6021	6/2/2013
PROMOGRAN PRISMA MATRIX	ETHICON INC (A JOHNSON & JOHNSON COMPANY)	MA028	A6021-22	4/27/2005
PROMOGRAN PRISMA MATRIX	ETHICON INC (A JOHNSON & JOHNSON COMPANY)	MA123	A6021-22	4/27/2005
PROMOGRAN PRISMA MATRIX WOUND DRESSING 4.34 SQ INCH HEXAGON	SYSTAGENIX WOUND MANAGEMENT (US) INC	MA028	A6021	6/2/2013
PROMOGRAN WOUND MATRIX DRESSING	JOHNSON & JOHNSON (A DIVISION OF ETHICON INC)		A6021-22	9/30/2002
PURACOL	MEDLINE INDUSTRIES INC	MSC8522	A6021-22	5/29/2007
PURACOL	MEDLINE INDUSTRIES INC	MSC8544	A6021-22	5/29/2007
PURACOL COLLAGEN MICROSCAFFOLD WOUND DRESSING	MEDLINE INDUSTRIES INC	MSC8522	A6021	6/2/2013
PURACOL PLUS	MEDLINE INDUSTRIES INC	MSC8622	A6021-22	3/30/2007
PURACOL PLUS	MEDLINE INDUSTRIES INC	MSC8644	A6021-22	3/30/2007
PURACOL PLUS	MEDLINE INDUSTRIES INC	MSC861X8EP	A6021	6/3/2011
PURACOL PLUS	MEDLINE INDUSTRIES INC	MSC8622EP	A6021	8/26/2008
PURACOL PLUS	MEDLINE INDUSTRIES INC	MSC8622EP	A6021-22	8/26/2008
PURACOL PLUS	MEDLINE INDUSTRIES INC	MSC8644EP	A6021-22	8/26/2008
PURACOL PLUS AG	MEDLINE INDUSTRIES INC	MSC8722EP	A6021	9/22/2008
PURACOL PLUS AG	MEDLINE INDUSTRIES INC	MSC871X8EP	A6021	6/9/2011
PURACOL PLUS AG COLLAGEN MICROSCAFFOLD WOUND DRESSING WITH SILVER	MEDLINE INDUSTRIES INC	MSC8722EP	A6021	6/2/2013
PURACOL PLUS AG COLLAGEN MICROSCAFFOLD WOUND DRESSING WITH SILVER	MEDLINE INDUSTRIES INC	MSC871X8EP	A6021	6/2/2013
PURACOL PLUS COLLAGEN MICROSCAFFOLD WOUND DRESSING	MEDLINE INDUSTRIES INC	MSC8622EP	A6021	6/2/2013
PURACOL PLUS COLLAGEN MICROSCAFFOLD WOUND DRESSING	MEDLINE INDUSTRIES INC	MSC861X8EP	A6021-22	6/2/2013
SIMPURITY COLLAGEN 2" X 2" PAD	SAFE N SIMPLE LLC	SNS50002	A6021	5/19/2014
SKINTEMP	BIOCORE		A6021-22-23	8/17/1995
SKINTEMP II DRESSING 2" X 2" SHEET	HUMAN BIOSCIENCES INC	ST 1022	A6021	5/17/2013
SKINTEMP II DRESSING 3" X 4" SHEET	HUMAN BIOSCIENCES INC	ST 1002	A6021	5/17/2013
STIMULEN 1.25" X 1.25" SOLUABLE SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9601	A6021	8/9/2013
STIMULEN 1.5" X 2.5" SOLUABLE SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9602	A6021	8/9/2013
STIMULEN 2" X 3" SOLUABLE SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9600	A6021	8/9/2013
STIMULEN 4" X 4" SOLUABLE SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9610	A6021	8/9/2013
STIMULEN ENHANCED COLLAGEN GEL SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9600	A6021-22-23	7/17/2007
STIMULEN ENHANCED COLLAGEN GEL SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9601	A6021-22-23	7/17/2007
STIMULEN ENHANCED COLLAGEN GEL SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9602	A6021-22-23	7/17/2007
STIMULEN ENHANCED COLLAGEN GEL SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9610	A6021-22-23	7/17/2007
STIMULEN ENHANCED COLLAGEN GEL SHEETS	SOUTHWEST TECHNOLOGIES INC	ST9640	A6021-22-23	7/17/2007

A6024 **COLLAGEN DRESSING WOUND FILLER, STERILE, PER 6 INCHES**

Product Name	Manufacturer/Distributor	Model Number	HCPCS Code	Effective Begin Date
FIBRACOL COLLAGEN-ALGINATE WOUND DRESSING (FILLER)	JOHNSON & JOHNSON (A DIVISION OF ETHICON INC)		A6024	1/31/2001
FIBRACOL PLUS COLLAGEN WOUND DRESSING WITH ALGINATE (FILLER)	JOHNSON & JOHNSON (A DIVISION OF ETHICON INC)		A6024	1/31/2001

Appendix 6

Collagen
Representative Pricing

Appendix 6:

Collagen Representative Pricing

Product	Quantity	Dist per Box	Case Box	Dist. Per Each	Contract Each	Dist Cost Calc.	Distributors
DRESSING, COLLAGEN, PURACOL WITH AG, 8X8	50/CS	$3,470.32	50	$69.41	$34.70	$28.21	MSC8488
DRESSING, COLLAGEN, PURACOL, STRL, 2" X 2"	50/CS	$308.65	50	$6.17	$3.09	$2.51	MSC8522
DRESSING, COLLAGEN, PURACOL, STRL, 2" X 2"	1/EA	$7.61	1	$7.61	$3.81	$3.09	MSC8522H
DRESSING, COLLAGEN, PURACOL, STRL, 2" X 2"	10/BX	$69.78	10	$6.98	$3.49	$2.84	MSC8522Z
DRESSING, COLLAGEN, PURACOL, STRL, 4X4.25	50/CS	$787.82	50	$15.76	$7.88	$6.41	MSC8544
DRESSING, COLLAGEN, PURACOL, STRL, 4X4.25	1/EA	$19.93	1	$19.93	$9.97	$8.10	MSC8544H
DRESSING, COLLAGEN, PURACOL, STRL, 4X4.25	10/BX	$185.07	10	$18.51	$9.25	$7.52	MSC8544Z
DRESSING, COLLAGEN, PURACOL, STRL, 8X8	50/CS	$2,260.79	50	$45.22	$22.61	$18.38	MSC8588
DRESSING, COLLAGEN, PURACOL PLUS, ROPE	50/CS	$499.10	50	$9.98	$4.99	$4.06	MSC861X8EP
DRESSING, COLLAGEN, PURACOL PLUS, ROPE	10/BX	$114.21	10	$11.42	$5.71	$4.64	MSC861X8EPZ
DRESSING, COLLAGEN, PURACOL PLUS, 2X2"	50/CS	$428.02	50	$8.56	$4.28	$3.48	MSC8622EP
DRESSING, COLLAGEN, PURACOL PLUS, 2X2"	1/EA	$10.49	1	$10.49	$5.25	$4.26	MSC8622EPH
DRESSING, COLLAGEN, PURACOL PLUS, 2X2"	10/BX	$99.91	10	$9.99	$5.00	$4.06	MSC8622EPZ
DRESSING, COLLAGEN, PURACOL PLUS, 4X4"	50/CS	$1,098.26	50	$21.97	$10.98	$8.93	MSC8644EP
DRESSING, COLLAGEN, PURACOL PLUS, 4X4"	1/EA	$26.89	1	$26.89	$13.45	$10.93	MSC8644EPH
DRESSING, COLLAGEN, PURACOL PLUS, 4X4"	10/BX	$256.06	10	$25.61	$12.80	$10.41	MSC8644EPZ
DRESSING, COLLAGEN, PURACOL + AG, ROPE, 1X8	50/CS	$580.04	50	$11.60	$5.80	$4.72	MSC871X8EP
DRESSING, COLLAGEN, PURACOL + AG, ROPE, 1X8	1/EA	$13.58	1	$13.58	$6.79	$5.52	MSC871X8EPH
DRESSING, COLLAGEN, PURACOL + AG, ROPE, 1X8	10/BX	$130.40	10	$13.04	$6.52	$5.30	MSC871X8EPZ
DRESSING, COLLAGEN, PURACOL PLUS AG, 2X2"	50/CS	$499.23	50	$9.98	$4.99	$4.06	MSC8722EP
DRESSING, COLLAGEN, PURACOL PLUS AG, 2X2"	1/EA	$12.05	1	$12.05	$6.03	$4.90	MSC8722EPH
DRESSING, COLLAGEN, PURACOL PLUS AG, 2X2"	10/BX	$104.84	10	$10.48	$5.24	$4.26	MSC8722EPZ
DRESSING, COLLAGEN, PURACOL PLUS AG, 4X4"	50/CS	$1,559.68	50	$31.19	$15.60	$12.68	MSC8744EP
DRESSING, COLLAGEN, PURACOL PLUS AG, 4X4"	1/EA	$42.14	1	$42.14	$21.07	$17.13	MSC8744EPH
DRESSING, COLLAGEN, PURACOL PLUS AG, 4X4"	10/BX	$354.89	10	$35.49	$17.74	$14.43	MSC8744EPZ
DRESSING, PRISMA, COLLAGEN W/ORC, 4.34 SQIN	40/CS	$837.14	40	$20.93	$10.46	$8.51	J-JMA028
DRESSING, PRISMA, COLLAGEN W/ORC, 4.34 SQIN	1/EA	$21.22	1	$21.22	$10.61	$8.63	J-JMA028H
DRESSING, PRISMA, COLLAGEN W/ORC, 4.34 SQIN	10/BX	$208.49	10	$20.85	$10.42	$8.48	J-JMA028Z
DRESSING, PRISMA, COLLAGEN W/ORC, 19.1 SQIN	40/CS	$2,229.37	40	$55.73	$27.87	$22.66	J-JMA123

Appendix 6:

Collagen Representative Pricing

Product	Quantity	Dist per Box	Case Box	Dist. Per Each	Contract Each	Dist Cost Calc.	Distributors
DRESSING, PRISMA, COLLAGEN W/ORC, 19.1 SQIN	1/EA	$55.59	1	$55.59	$27.80	$22.60	J-JMA123H
DRESSING, PRISMA, COLLAGEN W/ORC, 19.1 SQIN	10/BX	$553.99	10	$55.40	$27.70	$22.52	J-JMA123Z
DRESSING, COLLAGEN MTRX, AG, BIOSTEP, 4"X4"	50/CS	$2,453.92	50	$49.08	$24.54	$19.95	UTD66800122CS
DRESSING, COLLAGEN MTRX, AG, BIOSTEP, 2"X2"	50/CS	$1,285.29	50	$25.71	$12.85	$10.45	UTD66800126CS
DRESSING, COLLAGEN MATRIX, BIOSTEP, 2"X2"	50/CS	$1,110.13	50	$22.20	$11.10	$9.03	UTD66800124CS
DRESSING, COLLAGEN MATRIX, BIOSTEP, 4"X4"	50/CS	$2,103.35	50	$42.07	$21.03	$17.10	UTD66800125CS
DRESSING BIOSTEP COLLAGEN MATRIX 4X4	10/BX	$421.76	10	$42.18	$21.09	$17.14	UTD66800125Z
DRESSING, PRMGRAN MTRX 4.34"X4.34"-CMOP	10/BX	$198.42	10	$19.84	$9.92	$8.07	IDN53PG004
DRESSING, PROMOGRAN, MATRIX, HEX, 2.25"X2"	40/CS	$722.55	40	$18.06	$9.03	$7.34	J-JPG004
DRESSING, PROMOGRAN, MATRIX, HEX, 2.25"X2"	1/EA	$18.35	1	$18.35	$9.18	$7.46	J-JPG004H
DRSG, PROMOGRAN, COLLAGEN W/ORC, 4.34 SQ IN	10/BX	$180.09	10	$18.01	$9.00	$7.32	J-JPG004Z
DRESSING, PROMOGRAN, MATRIX, HEX, 5"X4.25"	40/CS	$1,923.27	40	$48.08	$24.04	$19.55	J-JPG019
DRSG, PROMOGRAN, COLLAGEN W/ORC, 19.1 SQ IN	1/EA	$48.17	1	$48.17	$24.09	$19.58	J-JPG019H
DRESSING, FIBRACOL PLUS, 2INX2IN	72/CS	$518.42	72	$7.20	$3.60	$2.93	J-J2981
DRESSING, FIBRACOL PLUS, 2INX2IN	1/EA	$7.55	1	$7.55	$3.78	$3.07	J-J2981H
DRESSING, FIBRACOL PLUS, 2INX2IN	12/BX	$86.96	12	$7.25	$3.62	$2.95	J-J2981Z
DRESSING, FIBRACOL PLUS, 4INX4.375IN	72/CS	$1,211.44	72	$16.83	$8.41	$6.84	J-J2982
DRESSING, FIBRACOL PLUS, 4INX4.375IN	1/EA	$17.10	1	$17.10	$8.55	$6.95	J-J2982H
DRESSING, FIBRACOL PLUS, 4INX4.375IN	12/BX	$200.99	12	$16.75	$8.37	$6.81	J-J2982Z
DRESSING, FIBRACOL PLUS, 4INX8.75IN	36/CS	$891.15	36	$24.75	$12.38	$10.06	J-J2983
DRESSING, FIBRACOL PLUS, 4INX8.75IN	1/EA	$25.02	1	$25.02	$12.51	$10.17	J-J2983H
DRESSING, FIBRACOL PLUS,.375"X.75",ROPE	36/CS	$693.67	36	$19.27	$9.63	$7.83	J-J2984
DRESSING, FIBRACOL PLUS,.375"X.75",ROPE	1/EA	$19.53	1	$19.53	$9.77	$7.94	J-J2984H
DRESSING, BIOPAD, W/COLLAGEN, 3/BX, 168/CS Angelini	3/BX	$49.60	3	$16.53	$8.27	$6.72 a	ACH132622
DRESSING, COLLAGEN MTRX, AG, BIOSTEP, 4"X4"	50/CS	$2,453.92	250	$9.82	$4.91	$3.99	UTD66800122CS
DRESSING, COLLAGEN MTRX, AG, BIOSTEP, 2"X2"	50/CS	$1,285.29	250	$5.14	$2.57	$2.09	UTD66800126CS

Appendix 6:

Collagen Representative Pricing

Product	Quantity	Dist per Box	Case Box	Dist. Per Each	Contract Each	Dist Cost Calc.	Distributors
DRESSING, PRISMA, COLLAGEN W/ORC, 19.1 SQIN	1/EA	$55.59	1	$55.59	$27.80	$22.60	J-JMA123H
DRESSING, PRISMA, COLLAGEN W/ORC, 19.1 SQIN	10/BX	$553.99	10	$55.40	$27.70	$22.52	J-JMA123Z
DRESSING, COLLAGEN MTRX, AG, BIOSTEP, 4"X4"	50/CS	$2,453.92	50	$49.08	$24.54	$19.95	UTD66800122CS
DRESSING, COLLAGEN MTRX, AG, BIOSTEP, 2"X2"	50/CS	$1,285.29	50	$25.71	$12.85	$10.45	UTD66800126CS
DRESSING, COLLAGEN MATRIX, BIOSTEP, 2"X2"	50/CS	$1,110.13	50	$22.20	$11.10	$9.03	UTD66800124CS
DRESSING, COLLAGEN MATRIX, BIOSTEP, 4"X4"	50/CS	$2,103.35	50	$42.07	$21.03	$17.10	UTD66800125CS
DRESSING BIOSTEP COLLAGEN MATRIX 4X4	10/BX	$421.76	10	$42.18	$21.09	$17.14	UTD66800125Z
DRESSING, PRMGRAN MTRX 4.34"X4.34"-CMOP	10/BX	$198.42	10	$19.84	$9.92	$8.07	IDN53PG004
DRESSING, PROMOGRAN, MATRIX, HEX, 2.25"X2"	40/CS	$722.55	40	$18.06	$9.03	$7.34	J-JPG004
DRESSING, PROMOGRAN, MATRIX, HEX, 2.25"X2"	1/EA	$18.35	1	$18.35	$9.18	$7.46	J-JPG004H
DRSG, PROMOGRAN, COLLAGEN W/ORC, 4.34 SQ IN	10/BX	$180.09	10	$18.01	$9.00	$7.32	J-JPG004Z
DRESSING, PROMOGRAN, MATRIX, HEX, 5"X4.25"	40/CS	$1,923.27	40	$48.08	$24.04	$19.55	J-JPG019
DRSG, PROMOGRAN, COLLAGEN W/ORC, 19.1 SQ IN	1/EA	$48.17	1	$48.17	$24.09	$19.58	J-JPG019H
DRESSING, FIBRACOL PLUS, 2INX2IN	72/CS	$518.42	72	$7.20	$3.60	$2.93	J-J2981
DRESSING, FIBRACOL PLUS, 2INX2IN	1/EA	$7.55	1	$7.55	$3.78	$3.07	J-J2981H
DRESSING, FIBRACOL PLUS, 2INX2IN	12/BX	$86.96	12	$7.25	$3.62	$2.95	J-J2981Z
DRESSING, FIBRACOL PLUS, 4INX4.375IN	72/CS	$1,211.44	72	$16.83	$8.41	$6.84	J-J2982
DRESSING, FIBRACOL PLUS, 4INX4.375IN	1/EA	$17.10	1	$17.10	$8.55	$6.95	J-J2982H
DRESSING, FIBRACOL PLUS, 4INX4.375IN	12/BX	$200.99	12	$16.75	$8.37	$6.81	J-J2982Z
DRESSING, FIBRACOL PLUS, 4INX8.75IN	36/CS	$891.15	36	$24.75	$12.38	$10.06	J-J2983
DRESSING, FIBRACOL PLUS, 4INX8.75IN	1/EA	$25.02	1	$25.02	$12.51	$10.17	J-J2983H
DRESSING, FIBRACOL PLUS,.375"X.75",ROPE	36/CS	$693.67	36	$19.27	$9.63	$7.83	J-J2984
DRESSING, FIBRACOL PLUS,.375"X.75",ROPE	1/EA	$19.53	1	$19.53	$9.77	$7.94	J-J2984H
DRESSING, BIOPAD, W/COLLAGEN, 3/BX, 168/CS Angelini	3/BX	$49.60	3	$16.53	$8.27	$6.72 a	ACH132622
DRESSING, COLLAGEN MTRX, AG, BIOSTEP, 4"X4"	50/CS	$2,453.92	250	$9.82	$4.91	$3.99	UTD66800122CS
DRESSING, COLLAGEN MTRX, AG, BIOSTEP, 2"X2"	50/CS	$1,285.29	250	$5.14	$2.57	$2.09	UTD66800126CS

Appendix 6:

Collagen Representative Pricing

Product	Quantity	Dist per Box	Case Box	Dist. Per Each	Contract Each	Dist Cost Calc.	Distributors
DRESSING, COLLAGEN MATRIX, BIOSTEP, 2"X2"	50/CS	$1,110.13	250	$4.44	$2.22	$1.81	S UTD66800124CS
DRESSING, COLLAGEN MATRIX, BIOSTEP, 4"X4"	50/CS	$2,103.35	250	$8.41	$4.21	$3.42	UTD66800125CS
DRESSING BIOSTEP COLLAGEN MATRIX 4X4	10/BX	$421.76	50	$8.44	$4.22	$3.43	UTD66800125Z
POWDER, STIMULEN COLLAGEN 1 GRAM SWT	100/CS	$1,812.16	100	$18.12	$9.06	$7.37	SWTST9501
GEL, COLLAGEN, 1/2OZ TUBE, 15GRAM SWT	12/CS	$417.86	12	$34.82	$17.41	$14.16	SWTST9502
HYDROGEL, COLLAGEN, WOUN'DRES, 28GM, 1OZ Coloplast	36/BX	$288.60	36	$8.02	$4.01	$3.26	c COI1166
DRESSING, WOUNDERS COLLAGEN HYDROGEL Coloplast	1/EA	$8.29	1	$8.29	$4.15	$3.37	COI1166H
HYDROGEL, COLLAGEN, WOUN'DRES, 3OZ Coloplast	12/BX	$288.11	12	$24.01	$12.00	$9.76	COI7690
COLLAGEN, PARTICLES, MEDIFIL, 1GRAM 10ML Biocore	5/BX	$83.09	10	$8.31	$4.15	$3.38	BOOMF2001
DRESSING, WND, BILAYER MATRIX, 2X2, DIR ONLY Integra	5/PK	$25,624.10	5	$5,124.82	$2,562.41	$2,083.26	ir NRCBMW202
DRESSING, WND, BILAYER MATRIX, 4X5, DIR ONLY Integra	5/PK	$44,689.01	5	$8,937.80	$4,468.90	$3,633.25	NRCBMW405
MEMBRANE, AMNIOTIC, REVITALON, 1CM DOTS	1/EA	$1,141.94	1	$1,141.94	$570.97	$464.20	MSS6001
MEMBRANE, AMNIOTIC, REVITALON, 2X2 CM	1/EA	$1,042.14	1	$1,042.14	$521.07	$423.63	MSS6011
MEMBRANE, AMNIOTIC, REVITALON, 4X4 CM	1/EA	$3,100.04	1	$3,100.04	$1,550.02	$1,260.18	MSS6022
MEMBRANE, AMNIOTIC, REVITALON, 4X6 CM	1/EA	$3,232.03	1	$3,232.03	$1,616.02	$1,313.83	MSS6023
DRESSING, WND, BILAYER MATRIX, 2X2, DIR ONLY	5/PK	$25,624.10	5	$5,124.82	$2,562.41	$2,083.26	NRCBMW202
DRESSING, WND, BILAYER MATRIX, 4X5, DIR ONLY	5/PK	$44,689.01	5	$8,937.80	$4,468.90	$3,633.25	NRCBMW405
MATRIX, DURA, DURAL, PATCH, COLLAGEN, 4IN	1/EA	$3,881.51	1	$3,881.51	$1,940.76	$1,577.85	NRCDP1045
MATRIX, DURO, DURAL, SYN, COLLAGEN, 5INX7	1/EA	$5,582.23	1	$5,582.23	$2,791.12	$2,269.20	NRCDP1057
MATRIX, DURA, DURAL, PATCH, COLLAGEN, 1INX1IN	1/EA	$756.24	1	$756.24	$378.12	$307.41	NRCDP1011
MATRIX, DURA, DURAL, PATCH, COLLAGEN, 3IN	1/EA	$2,341.65	1	$2,341.65	$1,170.83	$951.89	NRCDP1033
MATRIX, DURA, DURAL, PATCH, COLLAGEN, 3INX3IN	1/EA	$2,446.58	1	$2,446.58	$1,223.29	$994.54	NRCDURS3391
Gentel Collagen 2x2	30/cs	172.5	30	$5.75	$2.88	$2.34	

Appendix 6:

Collagen Representative Pricing

Product	Quantity	Dist per Box	Case Box	Dist. Per Each	Contract Each	Dist Cost Calc.	Distributors
Gentel Collagen 4 x 5	30/cs	397.5	30	$13.25	$6.63	$5.39	