# HELICOLL COMPARED TO OTHER PRODUCTS

## HELICOLL™ COMPARISION WITH OTHER FDA APPROVED PRIME PRODUCTS:

**http://helicoll.com/pdf/Helicoll_comparison_with_other_FDA_approved_prime_products_table.pdf**

**Unique Benefits to Safety:**

All of the following aspects are well addressed with proper production and management documents to comply the Medical Product regulations.

(i) Periodic monitoring of the results of the risk analysis
(ii) Specification of materials, and manufacturing/special processing
(iii) Specifications, drawings and circuit diagrams for components, sub- assemblies and the complete product including packaging, where appropriate.
(iv) The specifications of the checks, tests and trials that are intended to be carried out as part of routine production
(v) The performances and compatibilities intended by the manufacturer
(vi) Labeling, including any instructions for use
(vii) Identification of 'shelf-life' reflected by any 'use by' date, or other 'lifetime' of the device(s)
(viii) Results of Bench Testing
(viii) Clinical data
(ix) Post market surveillance
(x) Documentation and reporting Design Changes

**Additional Non-clinical Benefits:**

HELICOLL is a better cost-effective product than most other advanced skin substitutes on the market. Also, the easy use, storage and long shelf life are all added features to the product.

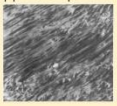
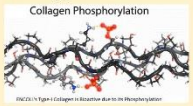
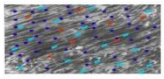
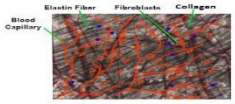
Our team of Wound Care specialists are extremely happy to assist your team of experts to bring the public awareness to the regenerative aspects of wound care that uses nanotechnology that bio-mimics the physiological biochemical pathways of wound healing process.

**Names of close Competitors:**

| | |
|---|---|
| ACell MS2550 | Q4134 hMatrix |
| MiMedx MS3680 | Q4135 Mediskin |
| Q4101 Apligraf | Q4136 Ezderm |
| Q4102 Oasis Wound Matrix | Q4150 Allowrap DS or Dry 1 sq cm |
| Q4104 Integra BMWD | Q4151* AmnioBand, Guardian 1 sq cm |
| Q4106 Dermagraft | Q4152* Dermapure 1 square cm |
| Q4107 GraftJacket | Q4153 Dermavest 1 square cm |
| Q4110 Primatrix | Q4154* Biovance 1 square cm |
| Q4111 Gammagraft | Q4160 NuShield 1 square cm |
| Q4115 Alloskin | Q4161 Bio-Connekt per square cm |
| Q4116 Alloderm | Q4163 Woundex, bioskin, per sq cm |
| Q4121 Theraskin | Q4164 Helicoll, per sq cm |
| Q4122 Dermacell, awm, porous sq cm | Q4165 Keramatrix, kerasorb sq cm |

| | |
|---|---|
| Q4123 Alloskin | Q4186 Epifix |
| Q4124 Oasis Tri-layer Wound Matrix | Q4195+ Puraply 1 sq cm |
| Q4126 Memoderm/derma/tranz/integup | Q4203 Derma-gide, 1 sq cm |
| Q4127 Talymed | Q4204 Xwrap 1 sq cm |
| Q4133 Grafix stravix prime pl sq cm | Q4221 Amniowrap2 per sq cm |

**117 MEDICARE-APPROVED SKIN SUBSTITUTES: PROPERTIES BY PRODUCT CATEGORY**

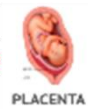
| PRODUCT ORIGIN | PRODUCT TYPE | PRODUCT DESCRIPTION | # of Total 117 | PRODUCT CLINICAL PROPERTIES |
|---|---|---|---|---|
| XENOGRAFT (ANIMAL ORIGIN) | EXTRACTED COLLAGEN SHEET | Helicoll<br>Patented Highly Purified, bioactive, non-immunogenic type-I collagen product. Helicoll's unique collagen scaffold with approx. 20µ Porosity and native staggered fibres.<br>  <br>  | 1 |  <br>Helicoll Bioactive type-I collagen attracts cells & factors in 1 to 3 days<br>  <br>Tissue regeneration in 4 to 5 days, not shown with other products<br>• Highly regenerative, phosphorylated, clinically effective, Type-I collagen. |
| | | Primatrix, Puraply, Integra & GraftJacket<br>Partially pure collagen mostly cross-linked with non-native, random distribution of fibres.<br>  | 12 | • Purification not patented.<br>• Random, non-native structural configuration.<br>• Freeze-drying results in matrix with average porosity > 800µ that is not conducive for ideal cell infiltration.<br>• Gamma sterilization is not ideal as it may denature and cross-link the protein resulting in lesser bioactivity. |
| | INTACT TISSUE DERIVED MEMBRANE | Oasis<br>Porcine Intestinal Wall<br>Cytal Wound Matrix<br>Porcine urinary bladder matrix<br>Mediskin<br>Porcine dermal and epidermal layer<br>Kerecis Omega3 Wound<br>Fish Skin | 7 | • All intact tissue membrane products, by default, contain immunogenic components like Elastin (approximately > 15% w/w) and Type-III Collagen etc.<br>• In case of Kerecis, chitosan is an additional contaminant.<br>• Kerecis with Omega3 Fatty acid may result in production of free radicals that damages tissue cells resulting in lesser regeneration.<br>• Direct or indirect cross-linking done to reduce their immunogenicity may constrain bioactivity.<br>• Restricted bio-effectivity and biological regenerative capabilities in the host tissue. |
| ALLOGRAFT (HUMAN ORIGIN) | | Alloskin, Alloderm, Dermapure, Truskin, Miroderm, Progenamatrix<br>Human Skin | 21 | |
| | | Amnion Bio, Biovance, Epifix, Restorigin, Woundfix Biowound, Xwrap<br>Amnion<br>Cellesta Cord & Surgicord<br>Umbilical Cord<br>Grafix, NuShield, Neopatch,<br>Placenta | 66 | |
| | | Apligraf & Dermagraft<br>Cell Seeded & Others | 10 | • Impaired bioactivity and biocompatibility. |

**What Differentiates Encoll's Helicoll product from the Competitors**:

Encoll has over thirty years expertise in the field of surgical applications of collagen. The founder and CEO of Encoll has technical contributions in the development of standards for manufacturing surgical grade collagen. This fact is evidenced by Dr. Gunasekaran's active involvement in the steering committee along with the FDA group headed by Dr. David Kaplan and other experts at ASTM (American Standards for Test Methods). Resulted in 1995 a ASTM as the guidelines to the manufacturers of Type-I collagen. (Ref: ASTM: F 2212–09 Standard Guide for Characterization of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products).

Encoll's expertise in the technical aspects of the development of non-immunogenic biological construct is enormous. Among the other fifty products in the market that are Medicare approved, almost half of them are manufactured from intact tissues. The manufacturers of such products are given authority to claim their products are "Biological skin substitutes". Unfortunately, these manufacturers don't realize that 15% elastin is still present in their final product which is NOT bio-compatible. Thereby, they have to cross-link the finished product to eliminate the rejection of those products. This action results in the loss of bio-activity for the entire product. This is the MAJOR difference when compared to Helicoll that is not

endpoint cross-linked in any manner.

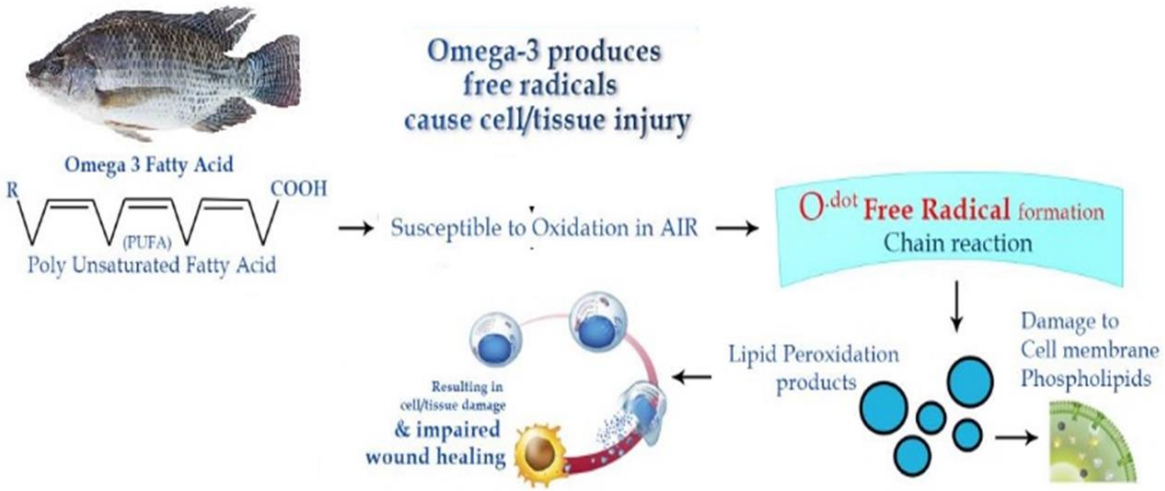
| ALLOGRAFT | XENOGRAFT |
|---|---|
| Grafix     Epifix XWrap | Oasis     Cytal |
| Intact tissue membrane products, by default contain immunogenic components like Elastin (approximately 15% w/w) and Type-III Collagen etc.<br><br>To reduce their immunogenicity, every product is directly or indirectly crosslinked which constrains the natural bioactivity of Type-I collagen.<br><br>Such restricted bio-effectivity of the Type-I collagen affects its natural biological regenerative capabilities in the host tissue. | |

Another set of products fall under the allograft category. The same hypothesis applies to these products where they produce an inferior outcome.

Another set of manufacturers who produce products with cultured cells are also having difficulties to manage the incompatibility or immunogenicity of certain structural proteins synthesized by those cells harvested from another individual. Furthermore, all such cell seeded products have an extremely high risk in maintaining sterility of their end product with a very short shelf life and an enormous cost of production.

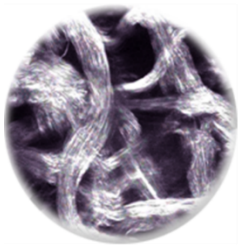
With respect to Piscean collagen, even the type-I collagen of a fish is not equivalent to that of human type-I collagen. It may not be biocompatible, as its amino acid sequence is not matching with that of a human type-I collagen (only 77.9% homology). On the other hand, Helicoll bovine type-I collagen is more biocompatible as it is 97.4% homologous to the human type-I collagen.

Piscean collagen also may have contaminating chitin (chitosan) possibly due to the remnants of scales in fish skin. Besides, the presence of Omega 3 fatty acids is more damaging to the tissues than its benefits. Fatty acids when stored in atmospheric air would release free radicals to damage the adjacent tissues.



I prefer the reviewer of this document to consider the pros and cons of intact tissue based skin substitutes. Both the recently approved innovative technology products namely ACell and MiMedx are derived from intact tissues. ACell MS2550 (derived from porcine urinary bladder) & MiMedx MS3680 (derived from amniotic tissue). Naturally all such intact tissue based products do have at least 15% of high immunogenic compound namely Elastin, besides other allergenic biological molecules like glycosaminoglycans and certain types of collagen other than type-I collagen.

Both the above products containing potential immunogenic molecules have to be surface charge modified (cross-linked) to minimize their immunogenicity. As a result, the above products are not capable to be a bio-active construct for faster healing and repair of the damaged tissues.



Other collagen preparations (ex. Puraply, Primatrix and Integra) as a result of lyophilization, yield random structural configuration that is non-native with avg. porosity > 800µ which is non-conducive for cell infiltration. Its bioactivity stays behind the bioactivity of sedimental preparation of HELICOLL type-I collagen that yields native parallel fibrils with porosity of approx. 20µ to attract more cells/regenerative factors. Additionally, Helicoll is EtO gas sterilized that does not denature the protein unlike gamma sterilization which is used by most other collagen preparations.
Collagen when cross-linked, the natural bioactivity may be significantly minimized.

**HELICOLL:**
On the other hand, Helicoll is nothing but highly bioactive and bio-compatible type-I collagen construct. That's why, Helicoll has been clinically documented for faster wound healing. (see the recent Stanford University Dermatology clinical study publication)
It encourages the formation of **new blood capillaries within 4 to 5 days** upon the application of the product over the wound.
**No other skin substitute has shown** such an advanced clinical result.