WHITE PAPER: Lyophilized Polymeric Collagen

1.0 PRODUCT INFORMATION

Material Name: Lyophilized Polymeric Collagen, Neutral pH
(Note: Type I Collagen from Tendon)

Product Number: FS32001 (sheet)
FS28003 (milled fibrous powder)

Product Description/
Appearance: Lyophilized sheet (pale and clean) or milled fibrous powder (passes 4 mm screen), supplied in bag at specified weight.

Product Analysis:

Test / Requirement	Specification
Moisture	< 12 % w/w
Purity*	>96 %
Gross composition	Typical analysis – TN 15.6%, Ash 0.6%, Lipid 0.6%
Amino acid analysis	Analysis shows typical profile
Heavy metals	Analysis provided (Antimony, Arsenic, Bismuth, Cadmium, Copper, Lead, Mercury, Molybdenum, Silver, Tin)
Collagen Type	Type I collagen (Types II and III not detectable)
Bioburden	Analysis provided – less than 200 cfu/g
Endotoxin	Analysis provided – less than 20 EU/g
Applicable standard	ASTM F2212 - 11 (Standard Guide for Characterization of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products)
Dispersion	Complete dispersion in 0.01 N HCl

* Purity is determined by composition analysis, absence of tryptophan, absence of collagens other than Type I, and content of hydroxyproline

Declarations: Each lot comes with:

- Supplier Declaration of disease free status of source material from New Zealand
- Government certification of the above where required by receiving country
- Certificate of analysis from an accredited independent laboratory

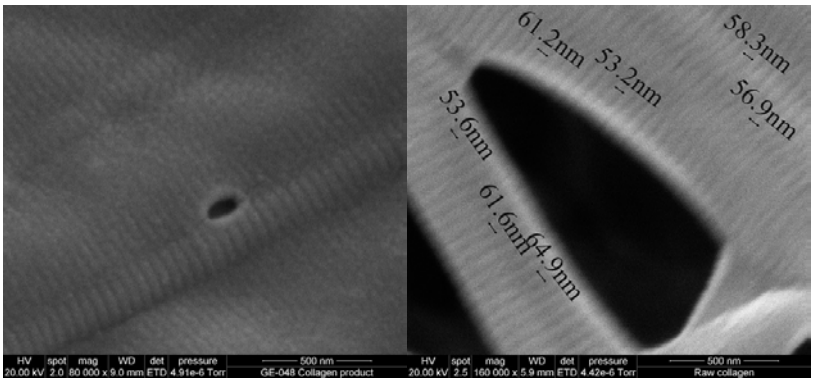

Figure 1: SEM images of the FS32001 (show typical D-space banding).

2.0 STORAGE REQUIREMENTS

Storage Conditions

Store at 2 - 8°C in low humidity environment

3.0 PRODUCT APPLICATIONS

This (polymeric) form of collagen retains its natural cross-linking. Additional cross-linking may be applied to adjust *in vivo* absorption time. This product is suitable for applications where natural strength is required, such as dental membranes and Bone Graft Substitutes.

Figure 2: Dental membrane (suitable for guided bone regeneration).

Figure 3: Bone graft substitute (contains osteo-conductive granules in mouldable form).*

*This product is characterized by mouldability and non-shedding of the osteo-conductive granules during moulding. These characteristics are achieved with a low-level addition of Type I polymeric collagen. Collagen Solutions proprietary technology which achieves these ends may be accessed through licensing or OEM manufacture.

4.0 SERVICE SUPPORT

Collagen Solutions provides support to our customers to address both technical questions and provide manufacturing advice. Common questions are around the various forms and solubility of Type I collagen (soluble or insoluble). These are addressed as follows:

Soluble Collagen

- Soluble collagen is extracted into dilute acid (pH 2) from the source tissue. The extracted molecules are in a triple helix form. When directly extracted in this way the collagen can be described as soluble telocollagen.
- In the source tissue many of the molecules are bound to each other by cross-linking across the ends, telopeptides, of the molecules. If, however, the tissue is also treated with pepsin, the telopeptides are digested by the enzyme. In this case, the yield of the extracted collagen is increased and the extracted collagen molecule can be described as soluble atelocollagen.
- Soluble collagen forms a clear solution in dilute acid but precipitates when the solution is neutralised to pH 5-7.

Insoluble Collagen

- Insoluble collagen is the product which remains when all material except the collagen is extracted from the source tissue. The collagen remains intact due to the cross-linking between the molecules.
- The insoluble collagen does, however, swell strongly in dilute acid.
- Insoluble collagen which has been swollen in dilute acid can be dispersed by application of mechanical energy and forms a clear solution.
- Dispersed insoluble collagen precipitates when the solution is neutralised to pH 5-7

Summary

- Soluble collagen is extracted from the source tissue
- Insoluble collagen remains when all other material has been extracted from the source tissue
- Both soluble and insoluble collagen are soluble in dilute acid (pH 2-3) and become insoluble when the solution is neutralised (pH 5-7).

The collagen which Collagen Solutions describes in this white paper is insoluble, or polymeric, collagen. Further detail and detailed video instruction on preparation of a solution of polymeric collagen and subsequent formation of a membrane are available through Collagen Solution's Commercial Managers.

5.0 REGULATORY SUPPORT

Collagen Solutions provides support to customers with both provision of information required by regulators and in responding to regulators questions. Because collagen is an animal sourced (xenograft) product regulators do have questions in addition to those required for any medical device. Bovine sourced collagen has a long record of safe use and the regulatory requirements are well established.

Collagen Solutions will typically provide, for regulators, a set of documents which address:

- The source and health of the animals used to manufacture the collagen and demonstrate how product safety is maintained throughout the supply chain (ISO 22442-2)
- The identity and safety of the collagen. (ASTM F2212 2011) The dossier includes a virus clearance study. (ISO 22442-3)

The full dossier is provided following commercial commitment to supply. Other support includes logistical services which meets country specific requirements for transporting animal-sourced products across borders.

6.0 REFERENCES

F.S. Steven and D.S. Jackson. Purification and amino acid composition of monomeric and polymeric collagens. *Biochem. J*. (1967) 104: 534–539

Brown, et al. Polymeric Collagen Biomaterials. US8785389 (2014)