



Standard Guide for Characterization and Standardization of Polymerizable Collagen-Based Products and Associated Collagen-Cell Interactions¹

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INTRODUCTION

The collagen family of proteins represents the major structural and mechanical component of the *in-vivo* extracellular matrix of human tissues and organs. Type I collagen is the most abundant and as such, it is an ideal candidate for medical materials, tissue-engineered medical products, delivery of therapeutic cells/molecules, and *in-vitro* cell/tissue culture applications. Furthermore, it is now evident that specific collagen material properties, including microstructure, mechanical integrity (stiffness), cell adhesion, and biodegradation are major determinants of the interfacial properties between cells and collagen-based materials, including guidance of fundamental cell behaviors that contribute to recapitulation and/or restoration of tissue structure and function. Advanced understanding of collagen self-assembly, as occurs *in vivo* and *in vitro*, is contributing to a rapid expansion of commercial and laboratory-produced collagen formulations that polymerize (self-assemble) or exhibit solution to gel (matrix) transition. Most recent developments have focused on collagen polymer formulations with tunable features to support the rational design of collagen materials for improved tissue integration and guidance of cell fate. Unfortunately, the term “collagen” is applied generally to describe various collagen types and formulations (soluble, insoluble, monomeric, atelocollagen) that vary significantly in their molecular compositions, self-assembly capacity and properties, and ability to interact with cells. As such, the need exists for an expanded set of characterization and standardization strategies to facilitate comparison, safety and efficiency testing, and translation of the next generation collagen polymer formulations and associated self-assembled collagen-based materials produced with these formulations.

1. Scope

1.1 This guide for characterizing polymerizable collagens is intended to provide characteristics, properties, test methods, and standardization approaches for use by producers, manufacturers, and researchers to identify specific collagen polymer formulations and associated self-assembled collagen-based products produced with these formulations. This guide will focus on the characterization of polymer forms of Type I collagen, which is the most abundant collagen in mammalian connective tissues and organs, including skin, bone, tendon, and blood vessels. Type I collagen may be derived from a variety of sources including, but not limited to, animal or cadaveric tissues, cell culture, recombinant, and chemical

synthesis. This guide is intended to focus on purified Type I collagen polymers as a starting material for wound and hemostatic dressings, surgical implants, substrates for tissue-engineered medical products (TEMPs), delivery vehicles for therapeutic cells or molecules, and 3D *in-vitro* tissue systems for basic research, drug development, and toxicity testing. Polymerizable or self-assembly implies that the collagen composition exhibits spontaneous macromolecular assembly from its components in the absence of the addition of exogenous factors including cross-linking agents. Self-assembling collagen polymers may include, but are not limited to: (1) tissue-derived atelocollagens, monomers, and oligomers; (2) collagen proteins and peptides produced using recombinant technology; and (3) chemically synthesized collagen mimetic peptides. It should be noted that the format of associated self-assembled collagen-based products also will vary and may include injectable solutions that polymerize *in situ* as well as preformed sheets, particles, spheres, fibers, sponges, matrices/gels, coatings, films, and other forms. This guide may serve as a

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