Amniotic Products: Liquid & Particulate

Overview

Human amniotic membrane grafting has been performed across many surgical specialties. It is immunogenic and has the potential to promote epithelial growth in addition to its anti-inflammatory, anti-microbial, and anti-fibrotic properties.[1] Amniotic products, tissue or membrane, are considered biologics and have been chiefly used as adjunctive treatment in orthopedic, wound, and ophthalmic procedures.[2-3] The amniotic membrane consists of an epithelial layer, a thick basement membrane, and mesenchymal tissue layer which are avascular, aneural, and alymphatic.[2-3] It offers a robust membrane for physical protection of the fetus from the surrounding maternal environment, a system for movement of fluids and nutrients, and containment of the amniotic fluid and fetus.[2,4] Secretion of a variety of molecules from the membrane signal antimicrobial and anti-inflammatory effects among other functions.[2-3]

Placental tissue is processed and can be used fresh or stored either as cryopreserved human amniotic membrane (CHAM) or as dry human amniotic membrane (DHAM).[2] CHAM must be maintained in its frozen state requiring specific transportation and storage conditions.[3] DHAM processes may reduce enzymatic activity and the viability of existing microorganisms.[3] DHAM can be used as a membrane or it can be cryomilled for particulate sizing (micronized) which can be reconstituted and administered as a flowable allograft.[3] The path for FDA approval and appropriate use for these products is variable based on intended use and how it is handled by the manufacturer. It is important to understand if the products utilized meet the FDA regulations.

Clinical Evidence

Evidence within this category comparing products, outcomes, and safety is limited and high-powered randomized controlled trials (RCT) or large meta-analyses are lacking. Studies available are primarily animal based or industry-sponsored. Human studies that have been performed are mainly small, case series, or pilot studies.

Food and Drug Administration (FDA) Guidance

Amniotic membrane and umbilical cord are considered structural tissues.[4] "Tissues that physically support or serve as a barrier or conduit, or connect, cover, or cushion in the donor are generally considered structural tissues…"[4] As such, they may be subject to regulation under the United States Food and Drug Administration (FDA) criteria for human cells, tissues, and cellular and tissue-based products (HCT/P's) outlined in PHS Act 361. These products require registration with the FDA. HCT/P's that do not meet the criteria for regulation under this act, including the requirements for minimal manipulation or homologous use, would fall outside of the standards and would likely be regulated as a drug, device, and/or biological product under section 351 of the PHS Act.[4]

An example of a minimally manipulated amniotic membrane is one that is processed to preserve and package it into sheets. This type of processing does not alter the function to serve as a barrier. However, if it is ground, lyophilized, and packaged as particles it is considered **more than minimally manipulated** because the processing alters the original characteristics to serve as a barrier.[4]

The amniotic membrane functions as a "…selective barrier for the movement of nutrients between the external and in utero environment, protecting the fetus from the surrounding maternal environment, and serving as a covering to enclose the fetus and retain fluid in utero."[4] This provides a basis for understanding homologous use of this product. When applied to the surface of the eye to cover or offer protection, it protects the eye from the surrounding environment, so the use would be considered homologous. A membrane that is used for bone tissue replacement to support regeneration or in wound healing to reduce scarring and inflammation is not aligned with the basic function of the amniotic membrane and would **not** be considered homologous use.[4]

In an effort to address public health and regulatory concerns regarding human cells, tissues, and cellular and tissue-based products (HCT/P's), the FDA created a tiered, risk-based approach within section 361 of the Public Health Service (PHS) Act (42 U.S.C. 264).[4] Title 21, Chapter I, Subchapter L, Part 1271 provides regulations for HCT/Ps and details the types of HCT/Ps that do not require premarket approval; as well as the registration, manufacturing, and reporting steps that must be taken to prevent the introduction, transmission, and spread of communicable disease by these HCT/Ps.[4]

Use of these products require an understanding of this section of Title 21 of the Code of Federal Regulations and other resources available from the FDA. Links to connect you with updated information are provided below.[5]

- Understand how the FDA defines HCT/P, minimal manipulation and homologous use Section 1271.3.
- Determine if a specific HCT/P falls within section 361 of the PHS Act and the requirements for registration refer to Section 1271.10.[5]
- If an HCT/P does not meet the criteria outlined in Section 1271.10 and a manufacturer does not qualify for the exceptions outlined in Section 1271.15 they are regulated as a drug, device, and/or biological product under section 351 of the PHS Act and must comply with the regulations outlined in section 1271.20.[5]
- Those who are able to register their HCT/P under the regulation must list all HCT/P's (including the established name and the proprietary name) that are recovered, processed, stored, labeled, packaged, distributed, or for which they perform donor screening or testing. Additionally, they must state whether each HCT/P meets the criteria set out in section 1271.10 of the regulations. Additional requirements for required information to be included in the listing are provided in section 1271.25.[5]
- The public can query The FDA Human Cell and Tissue Establishment Registration site to determine if an establishment is registered.[6]
- A flowchart regarding the application of the criteria in Title 21 for HCT/P's is located on page 6 of the FDA Regulatory Considerations for HCT/P document.[4]

References

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