Corcoran Consulting Group
a subsidiary of MEDICAL CONSULTING GROUP

REGULATION OF OPHTHALMIC AMNIOTIC MEMBRANE TISSUE

CORCORAN & CORCORAN

1 ***QUESTION:*** What is amniotic membrane tissue used for within eye care, and how do products differ?

ANSWER: It is donated human placental tissue configured as a biological bandage used to protect and promote healing of the ocular surface. It contains extracellular matrix components and, depending on the product and processing method, biologically active proteins and growth factors that reduce inflammation and encourage new cell growth.

Products differ by tissue preservation and processing (e.g., cryopreserved, dehydrated, or decellularized), configuration, physical design, handling, storage, FDA regulatory status, and Instructions for Use.

2 ***QUESTION:*** What is micronized amniotic membrane?

ANSWER: Micronized products process human amniotic tissue into particles or powder rather than intact grafts. They are generally intended for wound management or other non-ophthalmic applications, depending on the manufacturer's labeling and Instructions for Use. Non-ophthalmic products used in eye care pose serious regulatory and medicolegal concerns as well as not meeting Medicare's "reasonable and necessary" standard.[1]

3 ***QUESTION:*** What is a Request for Designation (RFD)?

ANSWER: An RFD asks FDA to determine the regulatory classification and lead FDA Center for a product. For companies producing amniotic membrane products, an RFD is a voluntary mechanism for determining whether §361 or §351 of the PHS Act applies. FDA's response to an RFD unambiguously declares a product's regulatory status.

4 ***QUESTION:*** What is the difference between §361 and §351 of the Public Health Service (PHS) Act?

ANSWER: In FDA terminology, HCT/Ps stand for Human Cells, Tissues, and Cellular and Tissue-Based Products. This category includes items like bone, skin, corneas, stem cells and amniotic membranes intended for human implantation, transplantation, or infusion. The FDA regulates HCT/Ps through a risk-based approach under 21 CFR Part 1271 dividing them into two main regulatory pathways depending on their processing and use.[2]

Section 361 HCT/Ps (*Minimal Regulation*):[3] If an HCT/P is minimally manipulated and intended for homologous use, meaning it performs the same basic function in the recipient as it did in the donor, it does not require FDA premarket approval. Manufacturers still register with the FDA, list their products, screen for communicable diseases, and follow strict manufacturing standards.

Section 351 Products (*Biological Drugs/Devices*):[4] If the product is more than minimally manipulated and heavily processed or not intended for homologous use, it is regulated as a biological product and requires FDA approval through a Biologics License Application before commercial licensing. Current Good Tissue Practices (CGTP) apply to establishments dealing with these products. FDA vigorously enforces relevant statutes and regulations.[5]

5 ***QUESTION:*** What is minimal manipulation?

ANSWER: Minimal manipulation refers to processing that does not alter the original relevant characteristics of a structural tissue (*e.g.*, bone or skin keeping its original strength and flexibility), or the relevant biological characteristics (*e.g.*, metabolic or endocrine functions) of cells/nonstructural tissues. Processing beyond this threshold may affect regulatory classification described above.[6]

July 14, 2026

Corcoran Consulting Group
a subsidiary of MEDICAL CONSULTING GROUP

REGULATION OF OPHTHALMIC AMNIOTIC MEMBRANE TISSUE

CORCORAN & CORCORAN

6 ***QUESTION:*** May one graft be divided among multiple patients?

ANSWER: No. Single-patient use supports sterility, tissue tracking, labeling, and regulatory compliance.[7,8] Sharing tissue between patients may also compromise traceability should a tissue recall or adverse event occur. Attributing expense to one or the other patient is a further problem.

Similarly, dividing one graft between two eyes of the same patient poses a billing conundrum because payment for each eye includes a whole graft.

7 ***QUESTION:*** Is off-label use of amniotic membrane permitted?

ANSWER: Yes, with caution. Off-label use refers to the use of products in a manner not specified in the package labeling.[9] Physicians may exercise independent medical judgment regarding off-label use, but manufacturers may not promote products beyond their cleared, approved, or otherwise authorized indications. From a compliance perspective, off-label use may increase professional responsibility because the physician should be prepared to justify the medical necessity, scientific rationale, informed consent, and standard of care for the treatment. Medicare generally excludes services that are experimental or investigational. Off-label use, by itself, does not establish that a service is experimental, but physicians should be prepared to demonstrate that the treatment is reasonable and necessary under applicable Medicare coverage policies.[1]

8 ***QUESTION:*** May a free sample be billed?

ANSWER: No.[10] Reimbursement typically requires a purchase or payment to validate the expense. A free sample is ineligible for payment because it is not a reimbursable expense as it does not involve a transaction where payment is made for the product.

A distinction is made between free samples and discounted products, as with a "Baker's Dozen"; the 13th item is not free, rather the lot is discounted 8%.

9 ***QUESTION:*** What are practical steps to take supporting regulatory compliance?

ANSWER:

- Follow the Instructions for Use of the product.
- Verify FDA regulatory status (§361 or §351), which may include a RFD, before using a product.[11]
- Maintain complete tissue tracking and documentation.
- Distinguish FDA regulation from Medicare reimbursement policy; they are complementary, not the same.
- Consult primary FDA, CMS and MAC authorities when uncertainty exists.

---

1 CMS. Medicare Program Integrity Manual, Chapter 13 §13.5.4 Reasonable and necessary provision. Link here.
2 21 CFR §1271. Link here.
3 PHS Act. Link here.
4 Ibid.
5 FDA. Letter to Amnio Technology, LLC. Link here.
6 21 CFR §1271.3(f). Link here.
7 BioTissue IFU. Link here.
8 DefEye IFU. Link here.
9 FDA. Link here.
10 OIG. Free Samples. Link here.
11 FDA RFD. Link here.

July 14, 2026