The FDA's 361 Exemption Rule and Its Application to Wound Care

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I. Executive Summary

The Food and Drug Administration (FDA) regulates Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) under a tiered, risk-based approach, primarily through Sections 351 and 361 of the Public Health Service Act (PHS Act). Section 361 grants the FDA the authority to issue regulations necessary to prevent the introduction, transmission, or spread of communicable diseases. In this section, certain HCT/Ps that meet specific criteria are exempt from premarket review, thus allowing for a different regulatory pathway compared to drugs, devices, or biological products that require rigorous premarket approval to demonstrate safety and efficacy. This exemption is referred to as the 361 exemption and is particularly relevant to wound care products derived from human tissues. For the manufacturers, this pathway can offer a swifter market entry and reduced regulatory burdens. However, it also comes with limitations, especially concerning marketing claims. For consumers, the 361 exemption may lead to quicker availability of certain tissue-based products, but it also raises concerns about the lack of premarket efficacy data. Recent regulatory updates from the FDA have signaled an intensified focus on ensuring accurate product classification and adherence to the 21 CFR Part 1271 (specifically, the 361 exemption criteria) by wound care product manufacturers, thereby influencing the market.

II. Introduction to the FDA 361 Exemption Rule

Section 361 of the PHS Act, enacted to protect public health, authorizes the FDA to establish and enforce necessary regulations to prevent the introduction, transmission, or spread of communicable diseases.1 This provision, originating in the 1990s, created a regulatory pathway for HCT/Ps that pose a lower risk to public health and, therefore, do not necessitate the intensive premarket approval required for higher-risk products.2 This contrasts with Section 351 of the PHS Act, which governs HCT/Ps that are perceived to have a greater potential for public health risk, thus requiring an Investigational New Drug (IND) application or a Biologics License Application (BLA) before they can be commercially sold.2 This two-pronged regulatory system, using both Sections 351 and 361, highlights the FDA's focus on risk. By doing this, the FDA can create a more efficient pathway for lower-risk products, mainly concentrating on preventing the transmission of communicable diseases.4

For an HCT/P to be regulated solely under Section 361 of the PHS Act and Title 21 CFR Part 1271, it must satisfy all of the following four key criteria:

First, the HCT/P must be **minimally manipulated**.4 The definition of minimal manipulation differs based on the type of tissue. For structural tissue, it refers to processing that does not

alter the original relevant characteristics of the tissue relating to its utility for reconstruction, repair, or replacement.4 Examples of processing steps generally considered minimal for structural tissues include antibiotic disinfection, decellularization, cryopreservation, sterilization, meshing, or cutting the grafts into smaller sheets.10 Even storage methods like refrigeration in a tissue medium or cryopreservation in liquid nitrogen vapor are typically considered minimal manipulation if they do not alter the original relevant characteristics.7 Conversely, processing that significantly alters the tissue's physical state or removes essential components can be considered more than minimal manipulation. For instance, homogenizing cartilage into a slurry or disaggregating collagen fibers in a ligament alters the original relevant characteristics.7 Similarly, grinding and lyophilizing amniotic membrane into particles or adding collagenase to adipose tissue for stromal vascular fraction (SVF) processing are also considered more than minimal manipulation.7 For cells or nonstructural tissues, minimal manipulation is defined as processing that does not alter the relevant biological characteristics of the cells or tissues.5 The determination of what constitutes minimal manipulation is therefore context-dependent, varying based on whether the tissue is structural or cellular/non-structural.5 This distinction is critical for manufacturers in accurately classifying their products.

Second, the HCT/P must be **intended for homologous use only**.4 Homologous use is when a recipient's cells or tissues are repaired, reconstructed, replaced, or supplemented with an HCT/P that performs the same basic function(s) in the recipient as it did in the donor.4 This intended use is determined by the manufacturer's labeling, advertising, or other indications of their objective intent. 5 In the context of wound care, examples of homologous use include using epidermal or amniotic tissue grafts intended for wound healing (as a cover or barrier) or dermal or epidermal grafts intended to reduce pain.4 The FDA also considers the use of amnion as a skin substitute for covering wounds to be a homologous use.10 Generally, tissues like bone, tendon, cartilage, ocular tissue, skin, and reproductive cells and tissues are considered 361 HCT/Ps if all criteria, including homologous use, are met.1 However, the FDA has clarified that using amniotic membrane for "wound healing" or to "reduce scarring and inflammation" is not considered homologous use, as these are not deemed basic functions of amniotic membrane.3 The FDA's interpretation of "homologous use" is therefore crucial and often subject to debate, especially concerning claims related to a patient's wound healing that extend beyond a fundamental cover or barrier function. Manufacturers must exercise caution in their product's labeling and their marketing must align with the FDA's definition.

Third, the manufacture of the HCT/P **cannot involve the combination of the cells or tissues with another article**, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of these agents does not raise new clinical safety concerns with respect to the HCT/P.5 This criterion aims to prevent the combination of 361 HCT/Ps with other active components like drugs or devices, ensuring their classification as primarily tissue-based products.5 This restriction helps maintain distinct regulatory pathways, as combining an HCT/P with a drug or device component that significantly alters its function or introduces new risks might necessitate regulation under a different framework that assesses the combined product's overall safety and efficacy.

Fourth, **either** the HCT/P **does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function** 5, **or**, if it does have a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, it must

be for autologous use, allogeneic use in a first- or second-degree blood relative, or reproductive use.5 This criterion addresses HCT/Ps with more complex biological mechanisms. The specified exceptions acknowledge particular situations, such as when the tissue is used within the same individual or closely related individuals, where the risk profile might be different. This reflects the understanding that using one's own tissue or tissue from close relatives may reduce the risk of adverse immune reactions or other complications.

The fundamental distinction between 361 HCT/Ps and products regulated under Section 351 of the PHS Act and the FDCA lies in the requirement for premarket review. HCT/Ps that meet all four criteria for the 361 exemption are not subject to premarket review or approval.1 Their regulation primarily focuses on preventing the transmission of infectious diseases under 21 CFR Part 1271.1 In contrast, products that do not meet all these criteria are regulated as drugs, devices, or biological products under Section 351 of the PHS Act and/or the FDCA.1 These products must undergo premarket approval, such as a BLA for biologics or a PMA or 510(k) clearance for devices, to demonstrate their safety and effectiveness.3 The 361 exemption offers a potentially faster route to market for specific tissue-based products, but it is accompanied by limitations on the types of products that can qualify and the claims that can be made about them.

Key Table 1: Criteria for FDA 361 Exemption for HCT/Ps

Criterion **Description** **Examples Relevant to Wound Care**

Minimally Manipulated For structural tissue: Processing that does not alter the original relevant characteristics related to utility for reconstruction, repair, or replacement. For non-structural tissue: Processing that does not alter relevant biological characteristics. Cutting skin grafts into smaller sizes 10, freeze-drying decellularized dermis 14, cryopreserving amniotic membrane.10 *Not:* Grinding amniotic membrane into particles 8, homogenizing cartilage.7

Homologous Use Repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function in the recipient as in the donor. Using split-thickness skin as a skin graft for covering wounds 10, applying amniotic membrane as a wound cover for protection.10 *Not:* Claiming amniotic membrane actively promotes wound healing or reduces scarring.3

Not Combined with Another Article Manufacture does not involve combination with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent that does not raise new clinical safety concerns. Skin graft stored in a buffer solution 7, amniotic membrane sterilized with ethylene oxide. *Not:* A wound dressing that incorporates an antimicrobial agent.24

Lack of Systemic Effect/Metabolic Dependence (or Exceptions) Either the HCT/P does not have a systemic effect and is not dependent on the metabolic activity of living cells for its primary function, OR if it does, it is for autologous use, allogeneic use in first- or second-degree blood relatives, or reproductive use. Acellular dermal matrix used as a wound cover 5, autologous skin graft.10 *Likely Not:* A cellular product intended to release growth factors systemically to promote healing (unless for autologous or close relative use).

Key Table 2: Regulatory Pathways for Wound Care Products

Product Category **Regulatory Pathway Premarket Review** **Focus of Regulation** **Examples**

361 HCT/Ps Section 361 PHS Act & 21 CFR Part 1271 No premarket approval required Prevention of communicable disease transmission; Donor eligibility and CGTP Amniotic membrane used as a wound cover 10, split-thickness skin grafts for covering.10
Medical Devices (e.g., Antimicrobial Wound Dressings) FDCA 510(k) (with special controls) or PMA Safety and effectiveness of the device Wound dressings containing silver 26, liquid wound washes with antibiotics.26
Biological Products Section 351 PHS Act & FDCA BLA Safety, purity, and potency (Less common for basic wound coverings; examples might include certain growth factors or complex cellular therapies, if used as wound treatments)

III. Wound Care Products and the 361 Exemption

The application of the 361 exemption criteria to wound care products requires a careful analysis of the specific characteristics of these products and their intended use. The "minimal manipulation" criterion is particularly relevant when considering tissues like skin, amniotic membrane, and other biological materials used in wound management.5 For structural tissues such as these, processing steps that preserve the tissue's inherent architecture and its ability to function as a physical barrier or provide a supportive matrix are generally considered minimally manipulative. For example, decellularization, a process used to remove cells while retaining the structural framework of the tissue, is often considered minimal manipulation for products like decellularized dermis intended for use as a wound covering.5 Similarly, freeze-drying and cutting these tissues into appropriate sizes for application to a wound are also typically viewed as minimal processing steps, provided they do not alter the basic characteristics of the tissue relevant to its role as a protective barrier.5 The critical aspect is that the processing should not change the original relevant characteristics of the tissue that contribute to its utility in providing a protective covering or structural support to the wound.5

The "homologous use" criterion is also central to determining whether a wound care product qualifies for the 361 exemption. Using skin as a skin graft to cover an area of skin loss, or applying amniotic membrane to a wound surface to act as a protective barrier, aligns with the definition of homologous use because these applications mirror the tissues' natural functions in a donor.4 The FDA has specifically recognized the primary function of amniotic membrane as providing a cover and protection.10 However, a critical distinction exists between using these products as a physical barrier and making claims about active wound healing processes, such as reducing scarring or exerting anti-inflammatory effects. The FDA often considers such claims to represent a non-homologous use because these are not considered the basic functions of these tissues in their native state.3 FDA guidance explicitly states that using an amniotic membrane for wound healing or to reduce scarring and inflammation does not meet the criteria for homologous use.3 Such interpretation significantly impacts how manufacturers can market their 361 HCT/P wound care products, as the claims must be carefully limited to reflect the tissue's inherent function as a barrier/cover.

Several categories of wound care products commonly fall under the 361 exemption, provided they meet all the specified criteria. These include tissue allografts such as split-thickness skin, dermis, and amnion products when they are intended for homologous use as a barrier or cover over a wound.10 For instance, dehydrated chorioamniotic membrane sheets used as wound covers are often regulated as HCT/Ps under Section 361.5 A wide array of skin and soft tissue substitutes, including products like Amniorepair, AmnioPlast, Amniotext, AMNIPLY, Apis,

Architect, ArdeoGraft, and Artacent Cord, may also be considered HCT/Ps, although their specific regulatory status under Section 361 would depend on their processing and intended use.28 In the context of burn treatment, examples of products classified as HCT/P 361 include cadaver skin, AlloDerm, EpiBurn, GammaGraft, and SkinTE.27 These examples illustrate the range of tissue-based products used in wound care that can potentially qualify for the 361 exemption if they adhere to the principles of minimal manipulation and homologous use, primarily serving as a cover or barrier to the wound environment.

IV. Wound Care Products Outside the Scope of the 361 Exemption

Many wound care products available on the market do not fall under the FDA's 361 exemption and are instead regulated as medical devices or drugs. This is particularly true for wound dressings, washes, and other products that contain antimicrobials or other active ingredients intended to have a therapeutic effect beyond simply covering or supporting the wound.4 These products are typically regulated under the Federal Food, Drug, and Cosmetic Act (FDCA) because their intended uses often involve preventing infection or actively promoting healing through pharmacological action, which goes beyond the basic function of human tissue as a barrier.24 Consequently, these types of wound care products generally require a 510(k) premarket notification with special controls or, in some cases, premarket approval (PMA) depending on their risk profile and the nature of their active ingredients.24

Recognizing the need for clearer regulatory pathways for these products, the FDA has proposed a new rule to reclassify certain types of wound dressings and liquid wound washes that contain antimicrobials or other chemicals as Class II or Class III medical devices.24 The proposed classification is largely based on the level of antimicrobial resistance (AMR) concern associated with the antimicrobials present in the product. For instance, wound dressings and liquid wound washes containing medically important antimicrobials, which are considered to have a high level of AMR concern, are proposed for Class III classification, potentially requiring a more rigorous PMA process.24 Conversely, products containing antimicrobials with a medium or low level of AMR concern might be classified as Class II devices, which would typically require a 510(k) premarket notification along with specific special controls.24 Manufacturers might face major changes under this proposed rule, potentially requiring them to comply with new labeling requirements, performance testing, and risk assessments for Class II devices, or to undertake the more extensive PMA process for Class III devices.24 Notably, the FDA has also proposed an exemption from the 510(k) requirement for certain liquid wound washes that contain only water or 0.9% saline and do not include antimicrobials, other chemicals, or animal-derived materials.24 The FDA anticipates that this proposed reclassification could lead to cost savings for both manufacturers and the agency by providing greater clarity in the regulatory submission process.25

Several examples of wound care products typically fall outside the scope of the 361 exemption due to the presence of active ingredients or claims that extend beyond homologous use. Wound dressings and liquid wound washes containing antimicrobials such as polymyxin B, silver sulfadiazine, and bacitracin are examples of products that may be proposed for Class III classification due to their high level of AMR concern.26 Products with antimicrobials like silver, zinc, copper, and chlorhexidine may be proposed for Class II.26 Additionally, various skin substitutes are cleared as 510(k) medical devices, including products like OASIS Wound Matrix, OASIS Tri-layer, and PriMatrix, which are acellular matrices derived from animal tissues.21

Other skin substitutes, such as Apligraf, Dermagraft, and Integra Dermal Regeneration Template/Omnigraft Dermal Regeneration Matrix, have undergone the more rigorous Premarket Approval (PMA) process.21 It is also important to note that even tissue-based products that might otherwise qualify for the 361 exemption could be reclassified and require premarket approval if they are marketed with claims that go beyond simply covering and protecting a wound, such as claims of actively promoting wound healing or reducing scarring.21 These examples illustrate that wound care products with active therapeutic agents or specific healing claims are generally subject to the medical device or drug regulatory pathways, rather than the 361 exemption.

V. FDA Oversight and Compliance for 361 HCT/Ps in Wound Care

Even though 361 HCT/Ps don't need premarket approval, companies making these products, such as those for wound treatments, still have obligations to ensure safety, primarily focused on preventing the transmission of communicable diseases. A key requirement is that manufacturers must register their establishments and list their HCT/Ps with the FDA using the electronic Human Cell and Tissue Establishment Registration System (eHCTERS).1 This registration and listing process provides the FDA with information about who is manufacturing these products and the types of tissues they are distributing, facilitating oversight and potential intervention if safety concerns arise.9 Manufacturers are required to update their listing at least every six months or whenever material changes occur in their HCT/P listing.1 However, certain exceptions to these registration and listing requirements exist, such as for establishments using HCT/Ps solely for nonclinical scientific or educational purposes, those performing same surgical procedure autografts, and carriers or shippers of HCT/Ps.16

In addition to registration and listing, manufacturers of 361 HCT/Ps for wound care must comply with stringent standards for donor eligibility and Current Good Tissue Practice (CGTP). For HCT/Ps recovered on or after May 25, 2005, a donor eligibility (DE) determination is mandatory, based on thorough screening and testing for relevant communicable disease agents and diseases (RCDADs).1 This includes screening donors for risk factors and clinical evidence of infection, as well as laboratory testing to detect evidence of infection.1 The CGTP requirements, outlined in 21 CFR Part 1271, Subparts C and D, encompass various aspects of manufacturing, including the methods, facilities, and controls used for recovery, screening, testing, processing, storage, labeling, packaging, and distribution of HCT/Ps.9 These regulations are designed to prevent contamination and damage to tissues, thereby minimizing the risk of disease transmission.1 Organizations like the American Association of Tissue Banks (AATB) also play a role in establishing and ensuring adherence to safety and quality standards within the industry.14

The FDA also maintains oversight of 361 HCT/Ps through post-market surveillance activities. Establishments that manufacture non-reproductive 361 HCT/Ps for distribution are required to investigate and report any adverse reactions involving communicable diseases and any deviations related to distributed HCT/Ps to the FDA.19 Subpart E of 21 CFR Part 1271 specifically addresses these non-reproductive 361 HCT/Ps and includes requirements for adverse reaction reporting and additional labeling.1 To ensure compliance with these regulations, the FDA conducts inspections of establishments that manufacture 361 HCT/Ps.16 In cases of non-compliance, the FDA has the authority to take various enforcement actions, including issuing Untitled Letters and Warning Letters, as well as orders for retention, recall,

destruction, and/or cessation of manufacturing, and even pursuing prosecution in severe cases.11 Specific labeling requirements also exist for HCT/Ps used in documented urgent medical need situations or those derived from ineligible donors.1 These measures demonstrate that while the 361 exemption waives the need for premarket approval, it does not equate to a complete absence of regulatory oversight. The FDA continues to monitor the safety of these products through post-market surveillance and enforces compliance with established regulations.

VI. The Benefits and Drawbacks of the 361 Exemption for Wound Care

The FDA's 361 exemption rule presents both advantages and disadvantages for manufacturers and consumers of wound care products.

For manufacturers, a primary benefit of the 361 exemption is the potential for expedited market access.5 Compared to the often lengthy and expensive premarket approval process required for drugs, devices, or biologics, the 361 pathway allows for a more rapid introduction of certain tissue-based wound care products to the market.5 This is largely due to the reduced regulatory burden, as manufacturers are not required to demonstrate safety and efficacy through extensive clinical trials before marketing their products.1 Consequently, manufacturers may also experience lower development costs associated with avoiding the need for extensive preclinical and clinical studies typically required for premarket approval.22 Manufacturers initially decide if their product meets the criteria for a 361 HCT/P. This can streamlined regulatory pathway can encourage faster innovation and potentially result in more competitive pricing for certain wound care treatments.

However, the 361 exemption also presents potential drawbacks for manufacturers. One significant limitation is on marketing claims; manufacturers of 361 HCT/P wound care products cannot make specific claims about wound healing that go beyond the tissue's basic function as a cover or barrier.10 There is also increased scrutiny from the FDA regarding whether a product truly meets the criteria for minimal manipulation and homologous use.3 If the FDA determines that a product does not qualify for the 361 exemption, manufacturers face the risk of enforcement actions, such as Warning Letters.11 Additionally, manufacturers of 361 HCT/Ps may encounter challenges in obtaining reimbursement from payers, who might require more robust evidence of efficacy, often derived from clinical trials.10 The lack of formal FDA approval or clearance for 361 HCT/Ps can also impact market perception and potentially reduce physician confidence in these products compared to those that have undergone premarket review.10

For consumers, the 361 exemption offers the potential for faster access to certain tissue-based wound care products that might not be available if subjected to lengthy premarket approval processes.22 This can lead to a wider range of treatment options for individuals suffering from chronic or non-healing wounds.1

However, there are also significant concerns for consumers associated with the 361 exemption. The primary concern is it's lack of rigorous premarket efficacy data, and products marketed under this exemption are not required to demonstrate that they actually work on patients for their intended use.1 This can lead to the potential for misleading or unsubstantiated claims by manufacturers regarding the therapeutic benefits of their products.12 Consumers also face the risk of adverse events or a lack of effectiveness due to the absence of thorough premarket evaluation.11 There may be limited information available to both patients and healthcare

providers regarding the quality and consistency of these products, except what come from the manufactours. 10 Furthermore, treatments utilizing 361 HCT/Ps may not be covered by insurance because of the lack of demonstrated efficacy, potentially leading to significant out-of-pocket expenses for patients.10

Key Table 3: Benefits and Drawbacks of the 361 Exemption in Wound Care

Stakeholder	Benefits	Drawbacks
Manufacturers	Expedited market access 5	Limitations on marketing claims 10
	Reduced regulatory burden 1	Increased scrutiny from FDA 3
	Potentially lower development costs 22	Risk of enforcement actions 11
	Self-determination of 361 status 9	Potential challenges in obtaining reimbursement 10
		Lack of formal FDA approval/clearance impacting market perception 10
Consumers	Potentially faster access to treatments 22	Lack of rigorous premarket efficacy data 1
	Possibility of more treatment options 1	Potential for misleading claims 12
		Risk of adverse events or ineffectiveness 11
		Limited information on quality and consistency 10
		Potential lack of insurance coverage 10

VII. The Evolving Regulatory Landscape

The regulatory environment surrounding 361 HCT/Ps, including those used in wound care, is continuously evolving. Recent years have seen an increased focus by the FDA on enforcement trends to ensure that manufacturers are not improperly utilizing the 361 exemption for products that should undergo more rigorous premarket review.3 This heightened scrutiny is evident in the increasing number of Untitled Letters and Warning Letters issued by the FDA to companies marketing HCT/Ps, including those intended for wound care.3 The FDA is particularly vigilant regarding products that make claims beyond homologous use or that are considered to be more than minimally manipulated.3 The agency has also taken a firm stance on stem cell therapies and amniotic fluid products that are marketed for conditions beyond basic wound covering, indicating that such uses may not qualify for the 361 exemption.13 In an effort to provide greater clarity to manufacturers and other stakeholders, the FDA has been actively issuing guidance documents to further define the concepts of "homologous use" and "minimal manipulation".3 This increased enforcement activity and the ongoing efforts to clarify regulatory definitions suggest a more challenging regulatory landscape for manufacturers operating in this space.

A significant development in the regulatory landscape was the end of the FDA's enforcement discretion period on May 31, 2021.10 This period was intended to provide manufacturers with sufficient time to assess whether their HCT/Ps required premarket approval, such as an IND or BLA.10 With the conclusion of this period, the FDA has made it clear that it no longer intends to exercise enforcement discretion for HCT/Ps that require but lack the necessary premarket approval.17 Marketing a product that requires premarket approval without having obtained it is now considered unlawful.17 This shift signifies a stricter regulatory stance on HCT/Ps, including those used in wound care, and increases the potential risks for manufacturers who have not appropriately classified their products or obtained the necessary approvals.

It is also crucial to consider the interplay between FDA regulations and the reimbursement policies of payers, such as Medicare.23 While obtaining FDA clearance or approval, or even qualifying for the 361 HCT/P designation, allows a product to be legally marketed, it does not

automatically guarantee Medicare coverage.23 Payers often have their own criteria for determining whether a product or service is considered reasonable and necessary, and they may require evidence of efficacy, even for products that have received FDA clearance or fall under the 361 exemption.23 Coverage decisions can be significantly influenced by the availability of high-quality clinical evidence supporting the safety and effectiveness of a product.21 For example, some payers may consider certain amniotic fluid allograft products as experimental or investigational for orthopedic conditions, which can impact reimbursement.35 Medicare also issues local coverage determinations (LCDs) for specific types of products, such as skin substitute grafts and cellular and tissue-based products used in the treatment of diabetic foot ulcers and venous leg ulcers, which outline the conditions under which these products will be covered.21 Therefore, even if a wound care product qualifies for the 361 exemption, manufacturers must also consider the need for clinical evidence to support reimbursement and ensure market access.

VIII. Conclusion and Recommendations

In conclusion, the FDA's 361 exemption rule provides a distinct regulatory pathway for certain tissue-based wound care products that meet specific criteria related to minimal manipulation, homologous use, lack of combination with other articles, and limited systemic effect or metabolic dependence. This exemption offers manufacturers potential benefits such as expedited market access and reduced regulatory burdens. Products that commonly fall under this category include tissue allografts like split-thickness skin and amniotic membrane intended for use as a wound cover or barrier. However, wound care products containing antimicrobials or other active ingredients, as well as those making claims beyond basic wound coverage, are typically regulated as medical devices or drugs requiring premarket review.

Despite the benefits of the 361 exemption, manufacturers also face drawbacks, including limitations on marketing claims, increased FDA scrutiny, and potential challenges in securing reimbursement. For consumers, while the exemption may lead to quicker availability of some treatments, concerns remain regarding the lack of premarket efficacy data and the potential for misleading claims. The regulatory landscape for 361 HCT/Ps is evolving, with the FDA demonstrating increased enforcement activity and a stricter stance following the end of the enforcement discretion period. Furthermore, reimbursement policies play a critical role in the commercial success of wound care products, often requiring evidence of efficacy beyond FDA regulatory status.

Based on this analysis, the following recommendations are provided:

For manufacturers: Conduct thorough due diligence to ensure that wound care products intended for the 361 exemption fully meet all the specified criteria and maintain comprehensive documentation to support this classification. Exercise caution and precision in marketing claims, focusing solely on the homologous use of the tissue as a cover or barrier. Stay abreast of the latest FDA guidance documents and enforcement trends to ensure ongoing compliance. Recognize that clinical evidence may be necessary to support reimbursement decisions by payers.

For healthcare providers: Develop a comprehensive understanding of the regulatory status of the wound care products being used, particularly those marketed under the 361 exemption. Be mindful of the limitations associated with these products, especially regarding the lack of premarket efficacy data and the potential for unsubstantiated marketing claims.

For the FDA: Continue to provide clear and up-to-date guidance on the interpretation of "minimal manipulation" and "homologous use" specifically within the context of wound care applications. Maintain a proactive and consistent approach to enforcement to prevent the inappropriate use of the 361 exemption and to safeguard patient safety. Consider the broader impact of regulatory pathways on fostering innovation and ensuring patient access to effective wound care treatments.

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