July 17, 2023

Dear Healthcare Provider,

As your trusted partner in the space of human cellular and tissue-based products (HCT/Ps), we feel it is imperative that you are aware of the current landscape in regard to regulation of 361 HCT/P products. We continue to uphold the highest standard of compliance as we meet and exceed all applicable federal guidelines. Most importantly, Regenerative Labs is compliant with all regulations and our safe and effective products are, as always, available to you and your patients.

As a valued practitioner, please take a few minutes to read this update and our outlook moving forward. The future is bright, and our field is at an exciting place, as we're poised to not only continue making a positive impact, but to lead the way in ensuring tissue-based products remain available and accessible to your patients.

We are confident that we not only meet, but exceed, FDA standards and guidelines as stated below:

1. The HCT/P is minimally manipulated;
2. The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;
3. The manufacturer of the HCT/P does not 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 water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P;
4. and Either:
    1. i) The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
    2. ii) The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and:
        1. Is for autologous use;
        2. Is for allogeneic use in a first-degree or second-degree blood relative; or
        3. Is for reproductive use.

All of Regenerative's HCT/Ps are **minimally manipulated**. In relevant part, FDA regulations define minimal manipulation as "For structural tissue, processing that does not alter the original

relevant characteristics of the tissue relating to the tissue's utility for reconstruction repair, or replacement. . .." 21 C.F.R. 1271.3(f).

In fact, we have a long history of ensuring our products meet all required standards and guidelines for 361 status, including minimal manipulation and have published and provided the exact type of objective evidence of minimal manipulation the FDA has accepted for decades.

Regenative states unequivocally that its intent for its Wharton's jelly HCT/Ps is that they be used **for homologous use only**, and that objective intent is reflected in its labeling and all advertising or other such materials controlled by Regenative.

Homologous use does not require that the tissue be identical or that it be used in the same anatomic location (e.g., skin for skin only is not required); rather " ... a use of a structural tissue may be homologous even when it does not occur in the same location as it occurred in the donor." Instead, the operative inquiry is whether the HCT/P performs a same basic function in the recipient as it performed in the donor. The basic function of an HCT/P is what it does from a physiological point of view, i.e., the function commonly attributed to the HCT/P as it exists in the donor. FDA recently reiterated and clarified that the tissue's function (not anatomical location) is the focus and provided the following example, "[a]n acellular dermal product is used for supplemental support, protection, reinforcement, or covering for a tendon. This is homologous use because in both anatomic locations, the dermis provides support and protects the soft tissue structure from mechanical stress."

Far from a conduit, Wharton's jelly is a **structural tissue** providing cushioning and support to surrounding tissues. While the overall purpose of the umbilical cord as a fetal organ includes providing a conduit between fetal circulation and maternal circulation, that conduit is provided by a pair of umbilical arteries and the umbilical vein.

Within the umbilical cord, Wharton's jelly serves the important basic function of providing structural support and cushioning against compressive forces from the surrounding environment. While the **anatomical location** may differ, that basic function remains the same. Moreover, regardless of anatomical location, structural cushioning and support is the basic function intended to be served by Regenative's Wharton's jelly HCT/Ps, which can objectively be seen by the labeling and materials provided on Regenative's website.

HCT/P products that meet the factors listed under 21 CFR 1271.10(a), as Regenative's products do, are governed by current Good Tissue Practice, under Section 171. Current Good Manufacturing Practices overall do not apply to HCT/P products regulated solely under Section 361 because such requirements are not applicable to tissue-based products as opposed to drugs or biologics. Regenative has strong evidence that its Wharton's jelly based products are

both minimally manipulated and intended for homologous use only. Accordingly, While Regenative's products meet many of the cGMP regulations, the applicable regulations for Regenative's products are cGTP regulations, which Regenative meets and exceeds.

Regenative's products remain available for purchase and compliant with all federal guidelines. We are confident not only because of our superior standards, but because of strong scientific precedent backing our products.

Regenative's Commitment to the HCT/P Industry

HCT/Ps, particularly structural tissues, that are minimally manipulated and for homologous use have proven to be safe and effective throughout their history and have yielded a multitude of advancements in patient outcomes. Minimally manipulated birth tissue products have enjoyed a long and established history of safe and effective use.

This is well known in our field, and we have remained diligent in advocating for and protecting not just the HCT/P industry, but health care providers and patients who have come to rely on and benefit from our products.

Moving Forward

As we lead the path forward for our industry, you can support tissue-based products and their known positive patient outcomes, by continuing use of Regenative products. We look forward to continuing to serve you and your patients now and well into the future.

I am excited by the many advancements to come in our field. Our outlook is bright, and we will keep you periodically up to date.

If you have any questions, please feel free to email me personally at tyler@regenativelabs.com, or reach me by phone at 800-891-3452. I look forward to hearing from you.

Best regards,

Tyler C Barrett
Chief Executive Officer