SECTION-BY-SECTION SUMMARY

REGROW ACT

March 25, 2016

A. Section 1. Title. The title of the Act is "Reliable and Effective Growth for Regenerative Health Options that Improve Wellness" (REGROW Act).

B. Section 2(a). Current Pathways. Nothing in the Act is intended to alter the existing regulatory pathway FDA created for human cells, tissues, and cellular and tissue based products (HCT/Ps) as provided in 21 CFR Part 1271. Those regulations refer primarily to the practice of medicine allowing use of HCT/Ps without advance FDA regulatory approval as long as the products are "homologous" (perform the same basic function in the recipient and donor) and the HCT/Ps are "minimally manipulated" (processing does not alter their relevant biological characteristics). Entities using HCT/Ps must comply with FDA regulatory requirements concerning registration and listing, donor eligibility and current good tissue practices.

C. Section 2(b)(creating new 351B of PHSA). Conditional Approval. An expedited review and approval category is created for cellular therapeutics composed of human adult cells that fall outside of the HCT/P exemption above if the sponsor provides to FDA preliminary clinical evidence of safety (through an Investigational New Drug application) and a reasonable expectation of effectiveness (in a Phase I/II study). These products could be used conditionally while the sponsor conducts a Phase III clinical trial and seeks approval of a Biologics Licensing Application (BLA). If FDA provides conditional approval based on its review of safety and efficacy data, a cell-based therapeutic can be administered to patients for a 5-year conditional use period before a Biologics Licensing Application (BLA) is required.

D. Section 2(b)(creating new 351B(b) of PHSA). Additional Requirements for Conditional Approval. This conditional approval pathway may be used only if all the following safeguards apply:

1. The cells or tissues are adult human cells or tissues;

2. The cells or tissues do not provoke a significant unintended immune response in the recipient;

3. They are minimally manipulated for a non-homologous use (can perform a different function, or be used in a different part of the body; e.g., mesenchymal stem cells isolated from fat tissue can be used to repair knee cartilage); or can be more than

minimally manipulated, but not modified genetically (e.g., increased in number; allowed to differentiate to become other cell types; etc.);

4. Must be produced for a specific indication;

5. The cells or tissues are produced exclusively for a use that performs, or helps achieve or restore, the same, or similar, function in the recipient as in the donor;

6. Within 5-years of FDA conditional approval, the sponsor must submit a full BLA. If it is not approved by FDA, use of the cellular therapeutic must cease;

7. The sponsor must provide an Investigational New Drug application (IND), annual reports and adverse event reports during the conditional approval period;

8. The sponsor must submit an IND application for the treatment of patients during the conditional approval period; and

9. Conditional approval has not been granted to the sponsor previously for the same product for the same indication.

E. Section 2(c)(creating new 351B(c) of PHSA). Informed Use. An individual using these cell therapeutics during the conditional use period must be informed of the circumstances of its conditional use (e.g., limited studies without proof of efficacy; additional studies required).

F. Section 2(d)(creating new 351B(d) of PHSA). Stem Cell Banking. In order to be eligible to provide cells conditionally approved for use in cell therapy, cell banks must be compliant with good tissue practices and the other requirements of the HCT/P provisions of 21 CFR Part 1271.

G. Section 3. Medical Devices Used to Recover, Process or Deliver Cell Therapeutics. Medical devices used in cell therapeutics can be reviewed and cleared for use using the 90-day 510(k) substantial equivalence premarket approval pathway. Device classification for purposes of review and approval shall be based on the general use of these devices to harvest, deliver or process cells, and to sustain their viability and function. It should not be based on use only with specific types of cells, or for specific uses unless unique to the intended use of the device. The *de novo* process can be used to down classify a device if no predicate currently exists. Finally, the FDA Center for Biologics Evaluation and Research (CBER) will have primary jurisdiction of products that combine both cells and devices.

H. Section 4. Guidance and Amended Regulations. Within 1-year of enactment, FDA may issue guidance to help implement this cellular therapeutics pathway. Guidance should be

finalized within 1-year following close of the comment period. If FDA decides to implement the Act by regulation, it should use notice and comment rulemaking, with a proposed rule issued within 1-year of enactment and with a comment period of not more than 60-days. Final rules should be published not less than 30-days before they become effective. Within 90-days of enactment, FDA shall convene at least one public meeting concerning its regulatory policies related to the development of regenerative medical products.

I. Section 5. Standards. FDA will work with all the stakeholders to develop standards to insure regulatory predictability regarding manufacturing processes and controls for regenerative medical products.