ALLIANCE for Regenerative Medicine

Statement of Michael J. Werner
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Good afternoon. My name is Michael Werner. I am Executive Director of the Alliance for Regenerative Medicine (ARM). ARM is the preeminent global advocate for regenerative and advanced therapies and fosters research, development, investment and commercialization of transformational treatments and cures for patients worldwide. It is comprised of about 240 life sciences companies, academic institutions, clinical centers, patient advocacy groups, and investors who have come together to support research and product development in cell therapy, gene therapy, and tissue engineering, and other advanced technology sectors.

On behalf of ARM, I am pleased to speak today to provide the organization's views about the FDA's draft guidances related to human cells, tissues and cellular and tissue-based products.

ARM welcomes the publication of the draft guidances and commends the FDA for holding this public meeting. How FDA interprets the relevant provisions of the Food Drug and Cosmetic Act and applies its regulations is critically important to ensuring that safe and effective products reach patients as soon as possible.

ARM has provided written comments to the docket regarding the draft guidances. My comments today are a summary of key points.

In General

As the leading organization in the sector, ARM has a diverse membership who develop products across the spectrum regulated by FDA under these guidances. For example, ARM represents manufacturers of products regulated under Section 351 of the Public Health Services Act that require an FDA marketing authorization, as well as companies with products that are regulated under Section 361 of the Public Health Services Act that do not require a marketing authorization from FDA.

What all manufacturers have in common, however, is that they seek a clear and predictable regulatory pathway to market. In general, ARM believes that while the draft guidances are a positive step forward, they still leave some questions unanswered regarding interpretation of regulations. Consequently, ARM believes that when FDA finalizes these guidances, it should take actions to provide even more clarity. This could take several forms. Further clarification on requirements for product characterization and related claims allowed for each type of product (351 vs 361) would be helpful.

For instance, we urge FDA to publish more examples of how the key terms in the guidances – such as minimal manipulation and homologous use – will be applied to various technologies.

This would include, for example, when certain technologies such as adipose tissue would and would not be considered more than minimally manipulated and where "repair, reconstruction and supplementation" lead to findings of homologous use or not. Along with these examples, we urge FDA to provide detailed rationale to provide even more clarity about how products will be regulated.

In addition, ARM urges FDA to provide flowcharts to clearly demonstrate the Agency's thinking regarding evaluation of these products. This would give sponsors a step by step process to determine how their product will be treated. The Agency could supplement its regulations and guidance by including flowcharts to help developers navigate through these guidances and provide the Agency's assessment criteria in a logical sequence. We provided examples in our written comments.

Finally, we believe that FDA should look for ways to communicate a more detailed public summary of the rationale for its regulatory decisions. For example, the Tissue Reference Group (TRG) processes and decisions can be made more transparent. ARM urges FDA to add an Appendix to the draft guidances that details TRG decision making processes. It would also be useful to reference where the TRG recommendations are published. In general, ARM would encourage FDA to allow increased interactions with sponsors during the TRG process and the Agency should publish a more detailed summary on the rationale for each TRG classification recommendation. Moreover, the TRG website should be updated within one quarter of activity.

Specific comments on the Minimal Manipulation and Homologous Use Draft Guidelines follow.

Minimal Manipulation

Our comments address specific terminology and provisions. For example:

- ARM is concerned about the guidance's use of the term "main function" – not currently a term used in the regulations. If FDA is going to use the term 'main function' it needs to be properly defined and not just in a 'such as' manner.
- ARM would like the Agency to confirm that the previously released list of processing steps in the Preamble to the 21 CFR Part 1271 regulation (published in the Federal Register on January 19, 2001) remains the current Agency thinking. If the Agency thinking has evolved, we request that the draft guidance identify under what circumstances, if any, the criteria outlined in 2001 would not constitute minimal manipulation. Centrifugation should be specifically called out as a minimal manipulation except where it may affect relevant characteristics of the tissue being centrifuged. This would bring the FDA's guidance in line with the European Advanced Therapy Medicinal Products (ATMPs) guidance which is followed by most regulatory authorities.
- ARM believes the guidance should clarify (with more examples) at what level a tissue's structure must be preserved to be considered to be minimally manipulated. The guidance implies, but does not explicitly state, that the primary structure, including the load bearing properties of the tissue, may be changed so long as the underlying tissue structure is unaffected.

Homologous Use

- This Guidance contains a lot of precise terminology. Adding a Glossary with the definition of the key terms used in the Guidance may be helpful to provide further clarity on how these terms should be interpreted and understood. Alternatively, FDA could add a reference in the Guidance to the definitions provided in 1271.3, ensuring that these definitions reflect the Agency's current thinking.
- FDA should provide additional clarity on its decision to distinguish between structural and non-structural tissues and cells in its definition of homologous use.
- ARM is concerned that the definition provided in this document does not consider the "same basic function" in a way that is consistent with the draft guidance Preamble.
- We recommend the list of basic functions of amniotic membrane be expanded to include "covering and protecting".
- We recommend the FDA add another sub-section to define in detail how homologous use applies to HCT/Ps intended for wound healing, including examples.

ARM appreciates FDA's efforts to continually improve, clarify and update its guidance in this area. We remain ready to work with the Agency on these issues in the days ahead.

Thank you.