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**Comments Prepared for the
FDA Public Hearing on
Combination Products Containing
Live Cellular Components**

Presented by

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I appreciate the opportunity to present comments at this FDA Public Hearing on Combination Products. My perspective is from the viewpoint of tissue engineering and of an individual who heads an NSF-sponsored Engineering Research Center on tissue engineering, the Georgia Tech/Emory Center for the Engineering of Living Tissues. I also bring the experience of an individual who is a member of the FDA Science Board and last year chaired the external science review of FDA's Center for Devices and Radiological Health.

Tissue engineering, and I use this term in the broadest sense possible so as to include all of regenerative medicine, is an emerging technology and with this there is an emerging industry. This technology has an enormous potential and the opportunity to help patients in ways not previously possible. Yet the industry is in the process of being born. At last count there were 66 companies with 3000 employees and only 4 approved products.

Because of the fledgling state of this industry, some would say fragile state, it is even more important than normal that a regulatory process and pathway be defined which is as streamlined as possible, protecting the public interest, but at the same time making tissue-engineered products and strategies available in as accelerated way as reasonable to patients and through a least burdensome process.

This was considered last year by the CDRH External Science Review Committee. From these discussions there was a recommendation that combination products need to be regulated with a least burdensome approach which is predictable, timely, flexible, transparent, interactive, and effective.

In April we at Georgia Tech hosted a Medical Technology Leadership Forum Summit Meeting on "Defining a Regulatory Process for Combination Products." This meeting brought together leaders from FDA, industry, and the research community with public policy experts. Tissue engineering provided the examples of combination products, and out of the discussions which took place over the two-day meeting, it is clear that as a community we still have a long way to go. The result was a series of recommendations whereby FDA and the community could work together.

We all talk about combination products, I even use the term myself, and in using this term, we imply that it is simply a combination of a device and a drug or a device and a biologic. For some products this may be true; however, tissue engineered products are anything but simple, they should not be considered as simply combinations, they are very unique products, representative of the kind of products we will increasingly see as we move further into the 21st century.

In considering the proposals being discussed at this public hearing, I offer two examples which I hope will illustrate the complexity of the products that we are discussing today.

The first example is a series of products based on a platform technology where the first generation product is simply a scaffold, the second generation is a scaffold with either growth factors or chemotactic factors, and it is only in its third generation that cells are added. Is the proposal today one which would have these products regulated as a device in its first generation, possibly even in its second generation, but in the third generation version the jurisdiction will be transferred? This appears to be not only unwarranted, but an impediment to the evolution of this platform technology and the development of new products.

Furthermore, from the viewpoint of the regulation of a technology, is the key issue for the third generation product the addition of cells? The fact of the matter is that the critical element may still be the scaffold and how the design integrates the cells and the scaffold into a product. Certainly cells in a scaffold are far different from cells alone, and thus to evaluate the science and thus the technology requires knowledge not just of cells, not just of the scaffold and the material from which it is made, but of the integrated cell-scaffold structure.

A key issue of course is the role of the cells, and this brings me to my second example, a very specific one which is somewhat an expansion on my first

example. A company develops a tissue-engineered cartilage by seeding chondrocytes into a scaffold. The main role of cartilage is very much a structural one. The cells in this case are not important in the context of the initial function of this tissue engineered cartilage, but are important in maintaining the long term viability and structural function. In this case, how should this product be regulated and by what part of FDA?

Historically, FDA has assigned jurisdiction based on the primary mode of action or function of the product, not on its components parts. In fact, if one is to consider this example cartilage product in terms of its components, it would be difficult to determine the relative contribution of the cells as compared to the scaffold. One must consider the integrated cell-scaffold product, and it is clearly a structural product.

In regard to the proposed jurisdictional transfer, CDRH historically has reviewed a certain class of products. The proposal before us would result in the transfer of at least some of these products to CBER. Such a transfer of jurisdiction would appear to be unwarranted. In fact, the proposed transfer may serve as an impediment to the further introduction of tissue-engineered products, in particular those based on existing platform technologies.

This of course does not mean that the current situation cannot be improved. Real improvement, however, will require FDA to think "out of the box." Knowing FDA

as I do, I have the utmost respect for its staff. I also believe that I understand the limitations under which it operates. This includes the statutory limitations. As part of this I understand FDA's organizational limitations, and I do not believe that FDA is organized for the products of the 21st century. If in an emerging area like tissue engineering all FDA can do is "shoe horn" these products into the existing structure, then Congressional action may well be necessary.

The American public deserves much more. I thus urge FDA to shelve the proposal being considered today and enter into a constructive dialogue with the tissue engineering community. This process has begun, but it needs to continue. Together I believe that we can achieve a process designed for the complexities of tissue engineering, a regulatory process which is fair and one which will help bring these innovative products and approaches to patients in a least burdensome way.