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02N-0169

FDA Public Hearing:

Combination Products Containing Live Cellular Components

24Jun02

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TS14

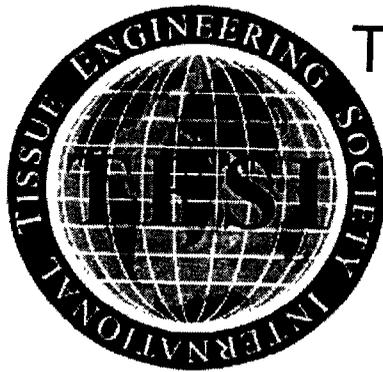
FDA Public Hearing:

**Products Comprised of Living Autologous Cells Manipulated
ex vivo and Intended for Implantation for Structural Repair
or Reconstruction**

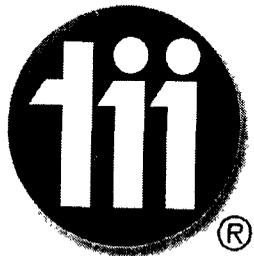
16-17Nov95



Pittsburgh Tissue Engineering Initiative, Inc.



Tissue Engineering Society International



Tissue Informatics, Inc.®

ASTM

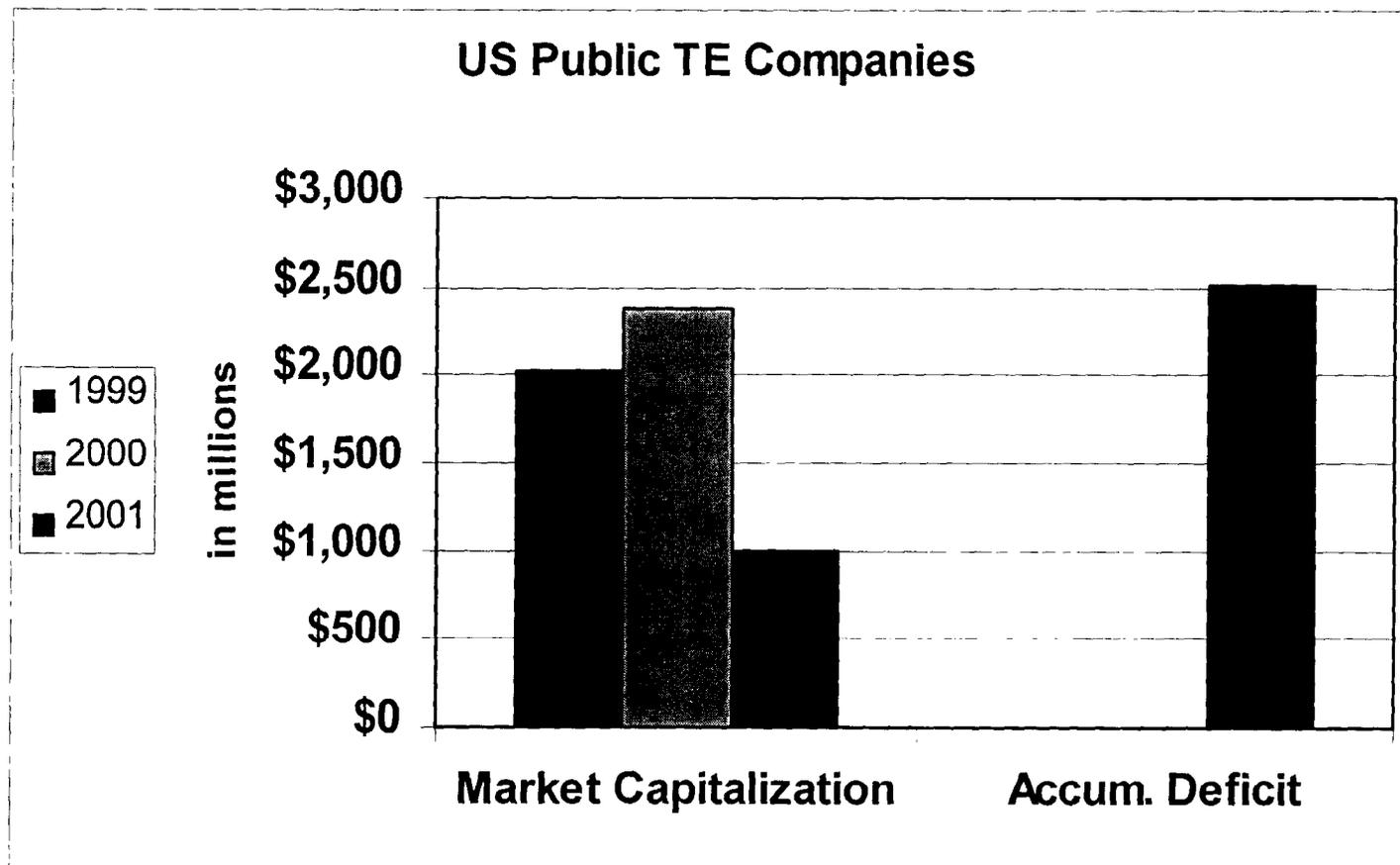
The Tissue Engineering Industry -- Today*

- **Since 1990, industry has grown to \$3.5 billion worldwide R&D effort****
- **Over 70 start-ups and business units**
- **16 publicly traded companies-- \$2.6 billion net capital value**
 - 78% U.S.; 22% Europe/Australia
 - Over \$600 million combined annual expenditure
 - Employ 3,300 scientists/support staff
 - Focus on structural applications (ex. skin, cartilage, bone, cardiac)

*M.J. Lysaght, J. Reyes, Growth of Tissue Engineering, *Tissue Engineering* 7(5), 485-493, 2001.

**Less than 10% funded by U.S. Federal government, but is increasing

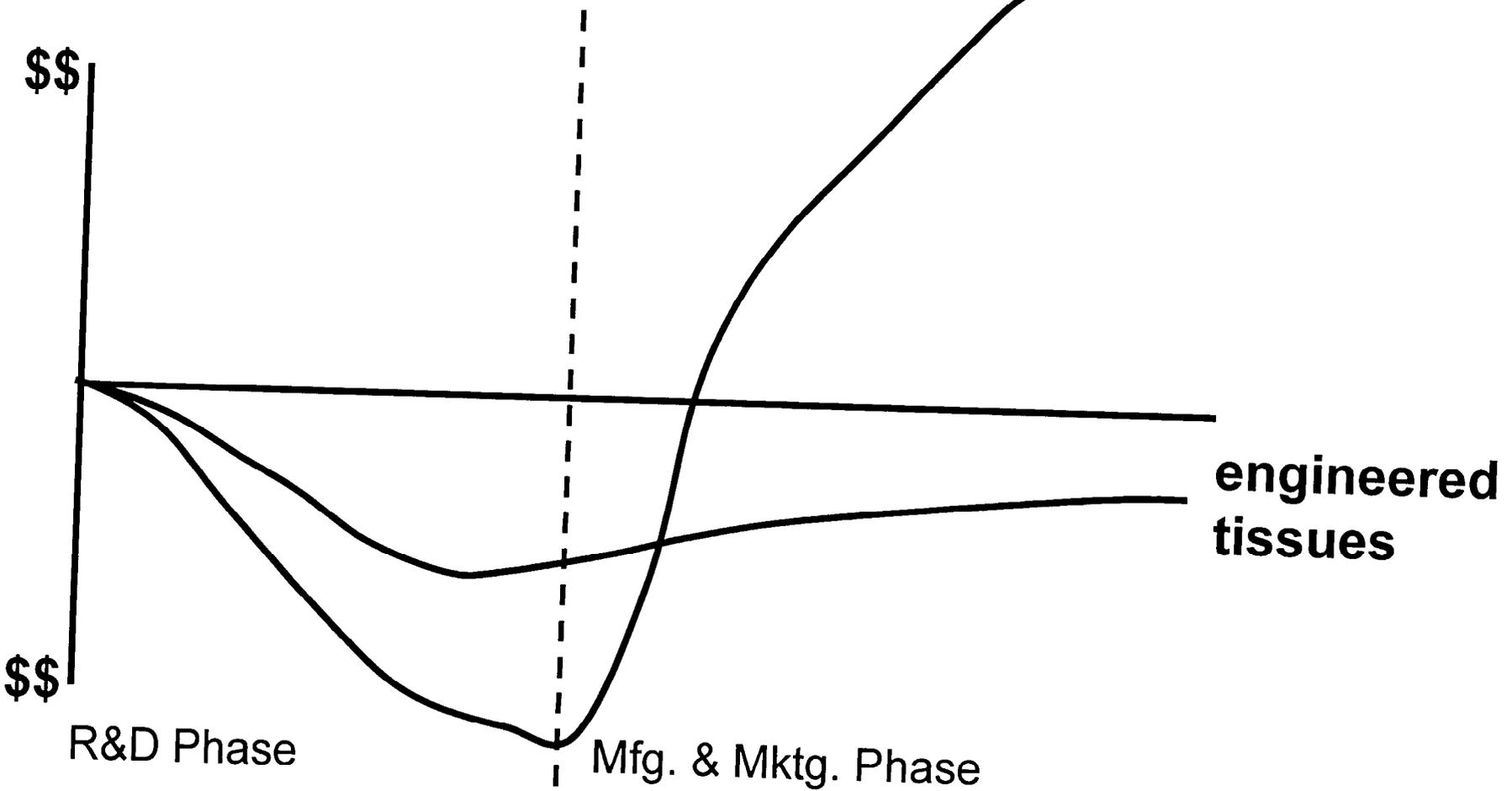
The Challenge of Market Acceptance



*1999 & 2000 figures from Lysaght study

The Challenge of Recovering R&D Costs

hypothetical comparable cost recovery



**Public/Private Financial Support for
Product Development**

**Value
Risk**

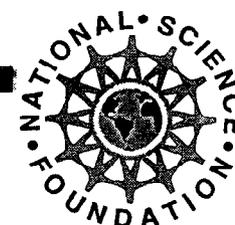
The Challenge of Financing Commercial Development

VALUE

economic: return on investment
societal: improvement in health

RISK

cost of market acceptance



WTEC Study on Tissue Engineering Research In Europe, Japan and the United States

Legal & Regulatory Issues

- **Lack of clear regulatory approval pathways across all major markets increases cost and time to market worldwide**

The Challenge of Regulatory Uncertainty

No Clear Path – Established approval paradigms not tasked for products incorporating living human tissues

Unpredictable Path – Approval paradigms established for products incorporating living human tissues not predictably applied

Fundamentally a classification problem

The Challenge of Applying Statutory Definitions to New Medical Technology

Devices



“ . . . An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar related article . . . Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease . . . or intended to affect the structure or any function of the body . . . **and which does not achieve any of its primary intended purposes through chemical action within or on the body . . . and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes**” FD&C Act, §201(h) (emphasis added)

Biologics



“ . . .any virus, therapeutic serum, toxin, anti-toxin, vaccine, blood, blood component or derivative, allergenic product, or **analogous product** applicable to the prevention, treatment or cure of diseases or injuries” PHS Act, §351(a)

Guidance on Applications for Products Comprised of Living Autologous Cells . . . Intended for Structural Repair or Reconstruction

28May96

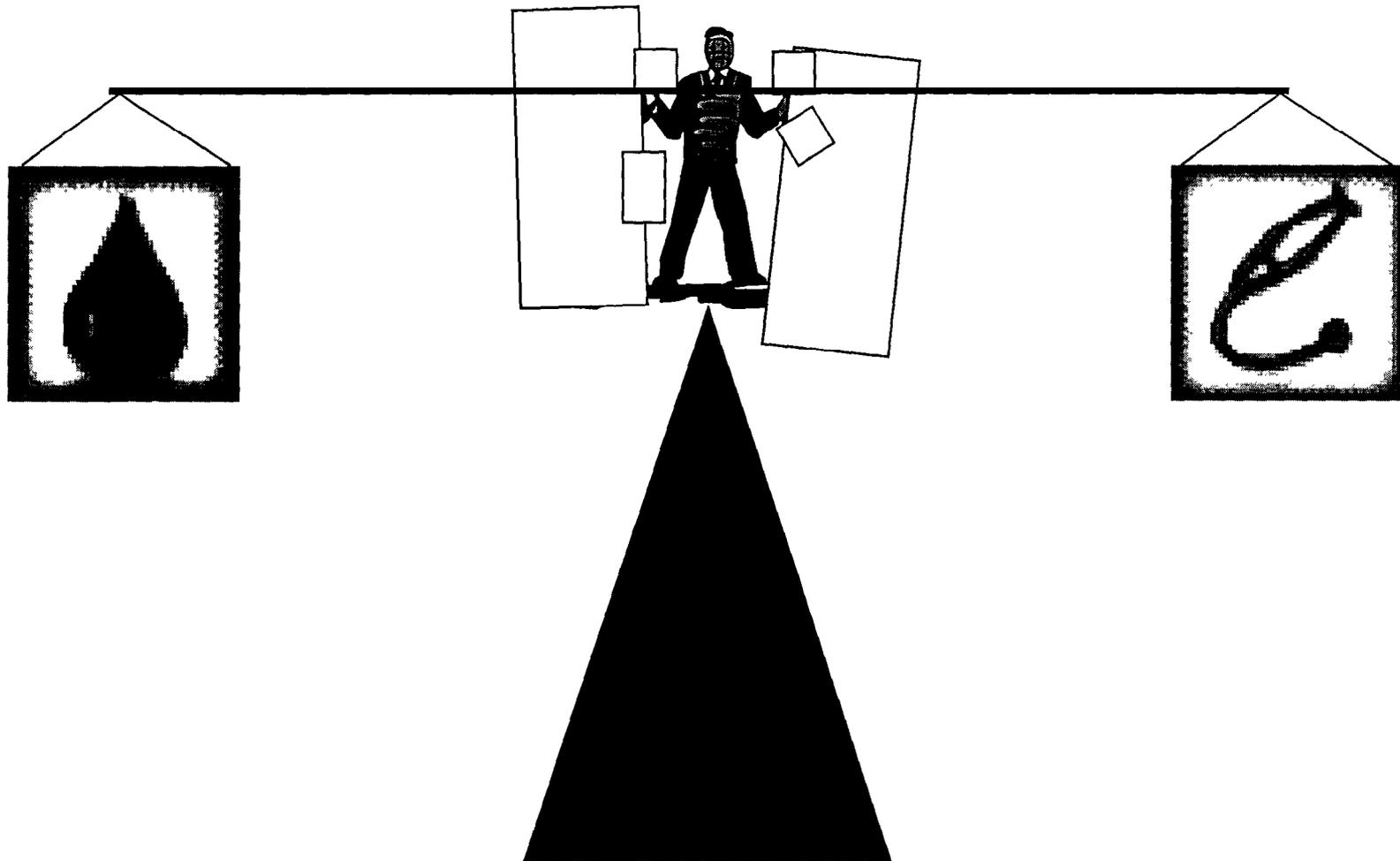
“ MAS cells products are dissociated from human tissue, and expanded ex vivo in order to provide sufficient number of cells for implantation, and thus would fall within the definitions for somatic cell therapy products. However, unlike systemic cellular therapies to treat malignant and infectious disease, the chondrocytes were implanted within an enclosed space, and thus had similarities to some tissue and device products.”

Proposed Approach to Regulation of Cellular and Tissue-Based Products

28Feb97

“Tissue-based products that are intended for diagnosis or therapeutic effect by physical action (including reconstruction or repair), and that contain synthetic or mechanical components, and achieve their primary mode of action by means other than metabolic or systemic action, are regulated as devices by CDRH.”

The Challenge of Uncertain Classification



Meeting The Challenge of Uncertain Statutory Classification

- **no immediate reclassification of approved products**
absent clear, compelling safety emergency
- **no reclassification of approved products**
absent clear, detailed classification rationale providing:
 - predictable entry point
 - predictable divergence points
- **moderate classification implications**
by true inter-center collaboration

Meeting The Challenge of Uncertain Statutory Classification

Inter-Center Collaboration --

**transcending assumption that medical product
is a combination of divisible parts susceptible
to serial regulation**

the multi-disciplinarity of Tissue Engineering

