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PhRMA's Perspective on Combination Products Containing Live Cellular Components

FDA Public Hearing
June 24, 2002

TS 16

“Potential Public Health Concerns as a Whole”

- Product Quality
 - Infectious agents
 - Tissue sourcing
 - Cross contamination during manufacture
 - Ancillary products
 - Manufacturing
 - GMPs - Process validation & controls, environmental controls, containment, product
 - Biological & Biomaterial component
 - Melding of these into a final product

“Potential Public Health Concerns as a Whole”

- Data demonstrating safety & efficacy
 - Well controlled clinical studies
 - Randomized, Blinded, Placebo Controlled - Ideal
 - Standard of Care
 - Controls may not be possible or appropriate
 - Flexibility appropriate to clinical application
 - Met vs. Unmet medical need
 - Fatal vs. Non-fatal

“Potential Public Health Concerns as a Whole”

- CDRH or CBER
 - Both charged with protecting the Public Health
 - Is there a greater public health risk with cell based wound healing products being regulated in CDRH?
 - Is there a greater history & expertise in regulating synthetic and biomaterials in CDRH?
 - Is there a greater history & expertise in regulating biological systems and their products in CBER?
 - Will cell based products & combinations become more complex?

“Given that Primary Mode of Action Determines Jurisdiction...”

- “Device Matrix” = A Cell Delivery System
 - Cells provide a “dynamic” environment promoting healing
 - Cytokines & Growth Factors, a.k.a., “Biologics”
- “The Matrix” optimizes the effect of the cells
- The Combination = Drug delivery system
 - a bio-reactor in situ
 - delivers a complex array of growth promoting factors

Evolution of Biological Product Regulation

- Past Biologic Products
 - Historically Complex & Difficult to Identify, Characterize, and Quantitate
 - Often Were Defined Primarily by Activity
- Specified Products
 - Peptides \leq 40 aa
 - Monoclonal Antibodies
 - Therapeutic DNA Plasmids
 - Therapeutic Recombinant DNA-derived Products

Biologic vs. Device

- FD&C Act Section 201(h)(1)(3)
 - any instrument, apparatus, ...implant
...intended to affect the structure or any
function of the body ... which *does not achieve
its primary intended purpose through chemical
action* within or on the body ... and which is
not dependent upon being metabolized for the
achievement of its primary purposes.

Biologic vs. Device

- PHS Act Sec. 351/CFR 600.3
 - Biological product means any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product or analogous product
 - Nothing in this act shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the FD&C Act

“information ... to determine...which
action is primary?”

- Efficacy dependent on chemical action or upon being metabolized vs. no such dependence
- Evaluate Matrix (the wound covering/barrier) alone vs. Matrix with Cells (the growth factor delivery system)
- When jurisdiction is not obvious:
 - Office of the Commissioner
 - Inter-Center expert panels
 - Advisory committees

PhRMA Recommendations

- Leave existing cell based wound healing products in CDRH
 - Ensures consistent review treatment as originally approved
- When non-wound healing applications of these products are proposed:
 - assign review based on mode of action, not historical approval mechanisms, claims (or lack of claims) to provide parity of regulation
 - e.g., angiogenesis in CAD
 - Gene therapies or growth factors vs. cell based wound healing dressing secreting angiogenic factors

PhRMA Recommendations

- Products containing living cells should be regulated within CBER's Office of Cell & Gene Therapy
 - Cells alone - for structure as well as function
 - Cells in a biomaterial/synthetic matrix
- “Matrix” components supporting cell delivery or function should be reviewed within CDRH in consult to CBER

PhRMA Recommendations

- Consistency of Regulation & Review
 - Jurisdiction:
 - Office of the Commissioner with representation from relevant Centers
 - Standardized & routinely updated Inter-Center Agreements (primary mode of action focus)
 - Process:
 - Equal accountability between lead & consult Centers

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