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THE REGULATORY CONTEXT FOR STERILITY STANDARDS IN CELL-BASED THERAPIES

NIST, April 19, 2022 Margaret Foster Riley J.D. (Virtual)





EVOLUTION OF FDA REGULATION OF CELL-BASED THERAPIES

- Originates with FDA regulation of gene therapy and tissue products in the 1980s
- FDA could have gone in a number of directions—but opted for a scheme that fit into the existing statutory framework and allowed flexibility as the agency gained experience with the technology



HUMAN CELLS, TISSUES OR CELLULAR OR TISSUE-BASED PRODUCTS—HCT/Ps

- Overlapping authority of the Food Drug and Cosmetic Act (FDCA) and Public Health Service Act (PHSA)
 - [this is true of Biologics generally]
- Congress has added additional aspects statutorily—mostly through the 21st Century Cures Act (2016)

PHSA § 361

- All HCT/Ps are subject to registration and good tissue practice requirements under §361 of the Public Health Service Act (PHSA):
 - *The Surgeon General, with the approval of the Secretary, is authorized to make and enforce such regulations as in his judgment are necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession. For purposes of carrying out and enforcing such regulations, the Surgeon General may provide for such inspection, fumigation, disinfection, sanitation, pest extermination, destruction of animals or articles found to be so infected or contaminated as to be sources of dangerous infection to human beings, and other measures, as in his judgment may be necessary.*
 - Gives the (FDA) broad powers because of expansive (and sparse) language

PHSA § 351

- Cells that undergo more than “minimal manipulation,” are combined with non-cell/non-tissue components, or used for non-homologous functions are regulated under §351 of the PHSA and the FDCA as biological drugs or devices that require premarket approval
- Good Tissue Practices and for products that qualify as biologic drugs or devices under §351 adds additional requirements for cGMPs

REGULATIONS

- 21 CFR Part 1271 - Human Cells, Tissues, And Cellular and Tissue-Based Products applies to both 361 and 351 products [developed by FDA in 2005 after some years of experience—superseded 1270.]
- “§ 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases.
 - “You must recover, process, store, label, package, and distribute HCT/Ps, and screen and test cell and tissue donors, in a way that prevents the introduction, transmission, or spread of communicable diseases.”
- These requirements do not require a specific methodology—the broad wording allows for significant flexibility

REGULATIONS

- 21 CFR Part 610 –Sterility Requirements that apply to all Biologic Products
 - Due to the nature of cell therapy products, FDA allows the sponsor to propose tests that are appropriate for their product.
 - The sponsor will be required to establish equivalence of these test methods to those described in 21 CFR 610 for licensure.

GUIDANCE

- Content and Review of Chemistry, Manufacturing, and Control (CMC) Information for Human Somatic Cell Therapy Investigational New Drug Applications (INDs) (2008)
- Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use; Guidance for Industry and Food and Drug Administration Staff (2017)
- Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry (2007)

ENFORCEMENT DISCRETION



A FOCUS ON FLEXIBILITY

- Biologics introduce numerous complexities that do not exist with small molecule drugs
- FDA has consistently resisted mandatory standards (e.g. USP monographs)
 - Tests themselves are complex
 - Patents may block other products

I THINK YOU SHOULD BE MORE SPECIFIC HERE IN STEP TWO



