Regulatory Implications for Global Manufacturing Development of Regenerative Medicines

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Disclosure

The views expressed in this talk are those of the presenter and not of Janssen R&D or Johnson & Johnson.

Themes for Today's Discussion

- Regulatory Framework
- Challenges and Opportunities
- Next Steps

Regulatory Framework

Regulatory Framework

Code of Federal Regulations
21 CFR 1270, 1271

Guidance
to Industry/ Reviewers

US Pharmacopeia
ICH Guidance

Example

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCHAPTER L--REGULATIONS UNDER CERTAIN OTHER ACTS ADMINISTERED BY THE FOOD AND DRUG ADMINISTRATION

PART 1271 -- HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS

Subpart D--Current Good Tissue Practice

§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.

Guidance for FDA Reviewers and Sponsors Content and Review of Chemistry, Manufacturing, and Control (CMC) Information for Human Somatic Cell Therapy Investigational New Drug Applications (INDs)

IV. Product Testing

A. Microbial testing

1. Sterility Testing (Bacterial and Fungal Testing)

A Test Method

Suitable sterility tests include the test described in 21 CFR 610.12 and the test described in United States Pharmacopoeia (USP) Sterility Tests (23rd edition, 1995) (Ref. 12).

USP<71>

- Media preparation
- Confirmation of Media sterility
- Media Storage
- Validation of the
- Sampling plans
- Minimum quantities of samples to be tested
- Handling of different types of samples
- Matrix interference test
- Observation & interpretation of results

"These Pharmacopoeial procedures are not by themselves designed to ensure that a batch of product is sterile or has been sterilized. This is accomplished primarily by validation of the sterilization process or of the aseptic processing procedures."

Challenges and Opportunities

Role of Critical Quality Attributes (CQA)

- Assuring consistency throughout development and marketing is a critical and complex regulatory and scientific challenge
  - Cells and gene vectors cannot be well characterized at the molecular level.
- Understanding product, mechanisms of action, and structure function relationships are key to determination of CQA and potency assay
- Understanding impact of process on product attributes, especially CQA
- Ensuring comparability of product throughout development so early results are still relevant
  - Role of CQA
  - Role of comparability protocols in ensuring consistency when process is optimized or up scaled
  - Role of process controls (including potentially, automated, closed processes)
  - Advantage of optimizing and locking down key parameters early

Challenges

- Sponsors have to interpret information from multiple sources, develop a comprehensive strategy to comply with the regulations and implement them in a Quality system
- Sponsors have flexibility in constructing their manufacturing control strategy within the regulations, however, once the strategy is implemented strict adherence is required as per GTP/GMP/GDP
- Non-standardized tests can increase costs and create inefficiency
- Information required in the IND may not inform reviewers about gaps in the Quality system

Opportunities

- Leverage Quality systems designed to be compliant with applicable regulations
- Regulators to provide feedback or assessment tools for Sponsors to understand if they are implementing the regulations and guidance appropriately
- Increase the number of pharmacopoeial monographs or have specific checklists for standardized/platform activities

Standard/Platform Activity

- Rapid mycoplasma and microbial testing for non-cryopreserved cell therapies
- Potency assay for CD19 CAR products
- Testing for residual process related impurities (BSA, proteases, foreign DNA)
- Information for risk analysis and setting specifications.
- Adenovirus, AAV and Lentiviral vector quality
- Monitoring replication competent virus

Next Steps

Commitment to Innovative Science

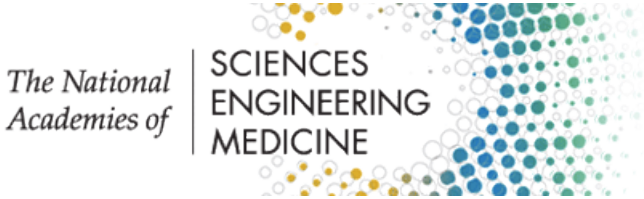
- ***Regulatory guidance*** should allow for ***flexibility*** in the development process and recognize and/or emphasize
  - iterative nature of the development process
  - need for a ***risk-based*** approach to development
  - differences in the product types

- Facilitation of global development of advanced therapeutics
  - ***harmonization/convergence*** of regulations, guidance and/or processes across a region(s)
  - consistency in the regulatory approval processes

Harmonization/Convergence

- ***Understand***
  - Regulatory gaps for advanced therapeutics between participating countries
  - What are the potential areas for harmonization/convergence
  - Potential to more effectively use standards
- ***Communication***
  - Regulators, Industry, Academia
  - Information necessary to enable discussions
  - Engage reciprocally in workshops, advisory committees, and working parties

Working Together!



- Education & Awareness
- Public Policy / Legislative
- Science & Technology
- Patients & Patient Advocacy
- Commercialization & Economy

Thank You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