Regulatory perspectives on Combination Therapy of Cancer

Steven Hirschfeld, MD PhD

Office of Cellular, Tissue and Gene Therapy

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Premise

- Education is required to minimize misperceptions and utilize existing regulatory mechanisms

Common Questions

- What is meant by the term “combination product”?
  - Regulatory definition: Two or more articles of different product types combined in particular ways outlined in the Code of Federal Regulations (21CFR3)

Common Questions

- How do FDA Centers coordinate review practice?
  - Designation of one Center as primary
  - Other Centers may perform a collaborative or consultative role. Precedent and mechanisms exist for each.
  - Sponsor submission of documents is only to the primary Center and Division. Internal sharing of documents is expected.

Common Questions

- How is an FDA Center chosen for a combination product?
  - If possible on the basis of primary mode of action, which is defined in the Code of Federal Regulations
  - If primary mode of action cannot be used, then the selection is based on precedents and experience with similar products
  - If no precedents exist, then the selection is based on expertise in the therapeutic questions

Common Questions

- What is expected to initiate a Phase I study with a combination product?
  - Following designation of a primary center, submission of an IND application
  - Pre-IND meetings are an option once the primary center has been designated
  - The FDA will internally arrange any collaborations or consultations

Common Questions

- What is expected to initiate a Phase I study with a multi-component product?
  - Submission of an IND to the FDA Center that regulates the type of product
  - Pre-IND meetings are an option once the primary center has been designated

Common Questions

- How are protocols submitted?
  - To the primary IND
- How are adverse events reported?
  - To the IND under which the protocol is filed

Common Questions

- Is there a need for single dose initial clinical studies for each component of a multi-component product or each product in a combination product?
  - Not necessarily. Factors include novelty of products, existence of prior clinical data from similar products, results of pre-clinical studies

Common Questions

- Does modification of one component of a multi-component product require filing a new IND?
  - Possibly. Determinations are made on a case by case basis.

Common Questions

- Can multi-component products and combination products qualify for incentives?
  - The usual programs of Fast Track, Orphan Status (with possibility of qualifying for development grants), Pediatric Exclusivity, Priority Review and Accelerated Approval can all apply using the relevant criteria

Summary

- Primary regulatory challenge may be a need for education of research community about definitions and programs