Regulatory perspectives on Combination Therapy of Cancer

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