

# ISBTC-FDA Meeting: Regulatory Breakout session

- Introduction and Presentation of Discussion Points – Jeffrey Weber
- Discussion
- Wrap-up and summary: Lex Eggermont
- Presentation at Dinner: Jeffrey Weber

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- What incentives exist to promote combination biologic therapies?
- The obvious incentive is efficacy, but if reagents are not made available to academic centers, no pre-clinical efficacy data will exist
- The first point is that companies need to make reagents freely available with proper protection of IP and confidence that confidentiality will be protected

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- Is there a role for private investment in pre-clinical research and clinical trials development; should we consider the Myeloma Consortium as a precedent to facilitate the testing of combinations that companies may not want to promote?

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- What can the FDA do to incentivize the testing of combinations:
  - What is the definition of a combination?
  - What laws, regulations and guidelines apply to combinations?
  - What does the Office of Combination Therapies do?
  - What Centers control the testing of combinations? How are jurisdictions settled?

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- What are the regulatory hurdles felt by Industry?
  - Who files the IND?
  - Who owns the BLA?
  - Who pays the user fee?
  - Whose NDA is it?
  - Is there a potential for antagonism?
  - Is there a need to show that each agent has a therapeutic effect?

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- What does the FDA have to deal with?
  - Are industrial partners reassured about IP protection and privacy?
  - Full disclosure is required to assess what information each partner has access to and what the FDA can disseminate to one or the other
  - What would be the effects of toxicity seen in a drug tested in combination on the use of that drug either alone or in other combinations?

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- What precedents do we have to look to?
- The approval of HIV combinations should be discussed as a case study.
- Pediatric drug development is also a paradigm for the development of combination therapies

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- What has NCI done to lessen the regulatory barriers?
  - Within UO-1 agreements, there are clauses to allow non-exclusive licensing
  - CTEP has promoted more than 100 combination LOIs
  - Companies need to be convinced that they should work with CTEP to develop their therapies in combination

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- Case discussions: Successful initiation
  - Combination therapy with protease inhibitor and anti-retroviral drugs
- Case discussions: Industry concern
  - Combination with an investigational vaccine and a novel investigational cytokine or adjuvant

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- Conclusions:
  - FDA and NCI have already laid the groundwork for testing and approval of combination biologic therapies; is education the primary challenge?
  - Lack of investigator support by industry, lack of awareness of protection afforded by the FDA, and reticence to reveal IP even if protected are major regulatory hurdles to the development of novel combinations of biologic agents