Regulatory Considerations

Multimodal Therapies for Brain Disorders

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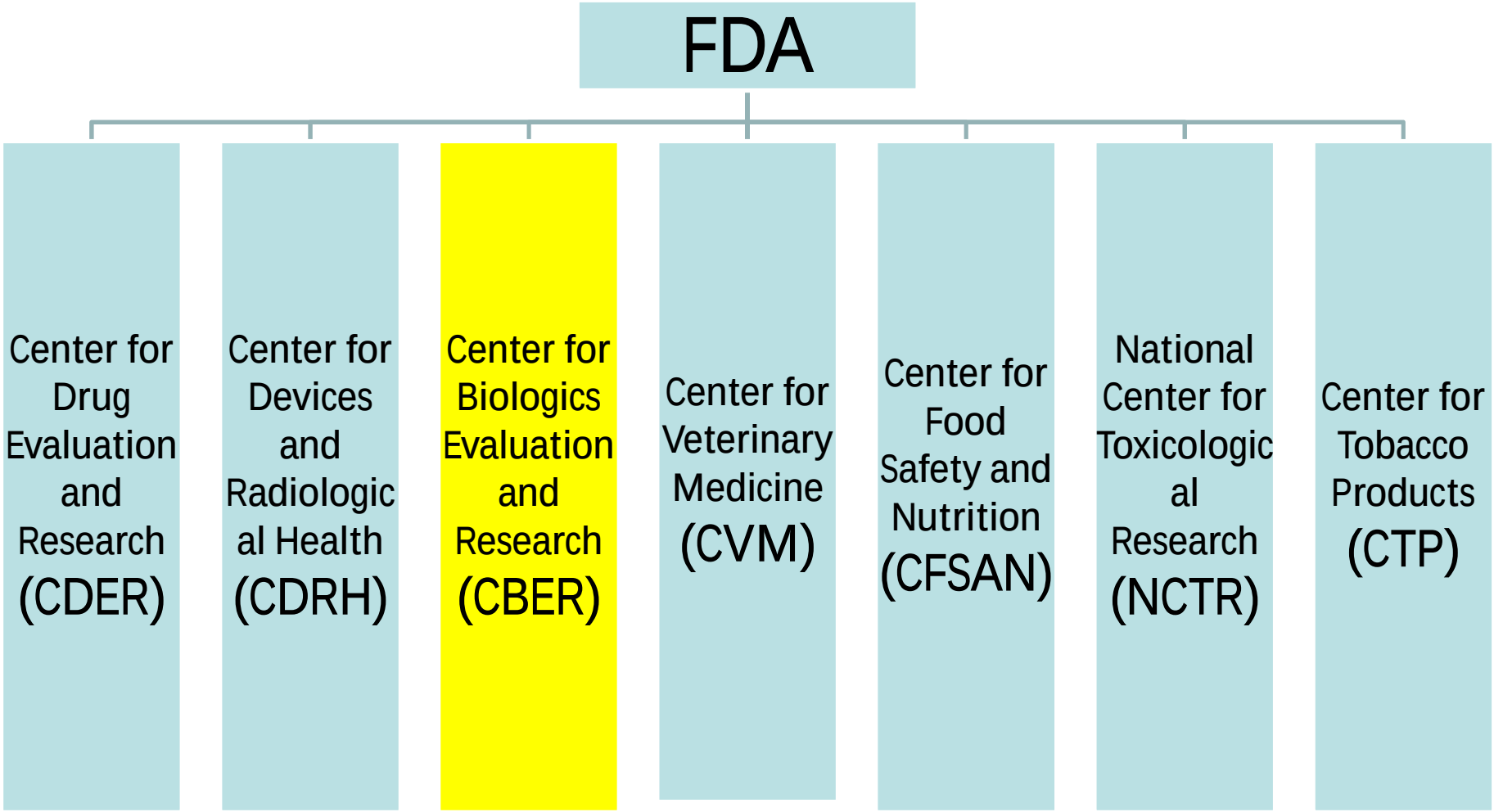

Not discussed in this presentation

1) Combination of a regulated drug or biologic (e.g., a cell or gene therapy) and a regulated device (e.g., for delivery of the cell or gene therapy)

2) Two therapies that are being investigated are not regulated by FDA

Two components are regulated and FDA-approved drug and biologic

Are the clinical investigations exempt from requirements for an Investigational New Drug Application (IND) (see 21CFR312.2)?

- Drug product is lawfully marketed in the United States
- The investigation
  - Is not intended as a well-controlled study to support a new indication for use or any other significant change in the labeling for the drug
  - Is not intended to support a significant change in the advertising
  - Does not involve a route of administration, dosage level, study population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the product
  - Is conducted in accordance with IRB requirements

Two regulated and investigational (i.e., not FDA-approved) drugs or biologics

- Each component must contribute to the safety and/or effectiveness of the combination
- "The amount and type of clinical data needed, and appropriate study designs will vary depending on the nature of the combination being developed, the disease or condition the combination is intended to treat, …"
- *Guidance for Industry: Codevelopment of Two or More New Investigational Drugs for Use in Combination* (2013)
- Consider a factorial design

Regulated Drug (or Biologic) and "Psychosocial Intervention"

What are the standards of evidence for a drug that is used concurrently with a psychosocial intervention?

- Substantial evidence of effectiveness of the drug
- Evidence of safety of the drug

Regulated Drug (or Biologic) and "Psychosocial Intervention"

Hypothetical: Drug (X) has proven safety and effectiveness when used in patients with Disease (Y) who were also receiving Psychosocial Intervention

What would be the labeling implications for Drug X?

- Relevant sections of the label include (but are not limited to):
  - Indications and Usage
  - Clinical Studies

Regulated Drug (or Biologic) and "Psychosocial Intervention"

What would be the labeling implications?

- Option #1
  - Indication statement: Drug X is indicated for treatment of patients with Disease Y who are receiving Psychosocial Intervention
  - Clinical Studies: The evidence of effectiveness (and safety) of Drug X comes from clinical trials in patients with Disease Y who were receiving Psychosocial Intervention

Regulated Drug (or Biologic) and "Psychosocial Intervention"

What would be the labeling implications?

- Option #2
  - Indication statement: Drug X is indicated for treatment of patients with Disease Y
  - Clinical Studies: The evidence of effectiveness (and safety) of Drug X comes from clinical trials in patients who were receiving Psychosocial Intervention

Regulated Drug (or Biologic) and "Psychosocial Intervention"

Would the Psychosocial Intervention be specified in the label Indication Statement?

Considerations:

1)What is the evidence of the safety and effectiveness of Drug X in the absence of Psychosocial Intervention?

2)Is the overall benefit-risk assessment for Drug X favorable or unfavorable in the absence of the Psychosocial Intervention?

Regulated Drug (or Biologic) and "Psychosocial Intervention"

Would the Psychosocial Intervention be specified in the label Indication Statement?

What if there are no data (or insufficient data) on the safety or effectiveness of Drug X in the absence of the Psychosocial Intervention

Considerations:

1) Are such data necessary prior to marketing approval?

2) Could collection of such data be a post-marketing requirement?

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