Approaches to Modeling Efficacy – Nonclinical Science

Advancing Regulatory Science for Medical Countermeasure Development: An Institute of Medicine Workshop

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Overview – Modeling Efficacy
Advancement of MCMs under the “Animal Rule”

Animal Models

Expected Clinical Outcome
What Regulatory Science Tools can be used to Shorten the Bridge?

- Confidence in predictability of models
- FDA “accepted” surrogate markers
- Nonclinical = clinical partnerships

• FDA Animal Rule is the key
  – ‘applying the Rule has become quite complicated’
    (Dr. Rosemary Roberts, FDA Public Meeting to discuss the Draft Guidance for the Animal Rule, Nov. 2010)

• Supporting Documents
Regulatory Science Tools –
What are the Gaps for Animal Models?

1. Consistently defining essence of the Animal Rule to product Sponsor
   – What is a “well-characterized” model? When is statistical significance really required? How to address perceived drug class effects?

2. Appropriate review based on risk and benefit
   – These are high risk life-threatening diseases
   – Identify means for FDA to accept a larger “leap of faith” when licensing MCM – different than more traditional vaccines or therapeutics b/c there is little clinical knowledge of these diseases
Regulatory Science Tools –
What are the Gaps for Animal Models?

3. Pre-competitive mechanism to share basic model information quickly
   – Shared proof-of-concept studies to avoid duplication (ex. - NIAID sponsored)

4. Ways to bridge nonclinical models to expected human outcome
   – Sponsors use of ‘FDA Accepted’ surrogate markers, correlates of protection, clinical observations in animals, pathology, etc.
1. Develop strategic plan for utilizing the Animal Rule
   – Finalize Draft Guidances (Jan ’09 and Oct ‘10) to reflect current thinking, and then apply consistently
   – Identify areas that can be “standardized” by disease and recognize those that cannot be
   – Prepare to accept more risk and mitigate it by special licensing conditions such as “restricted” or “conditional” for products intended for the Stockpile, but without other markets (HHS PHEMCE Review, Transforming the Enterprise to Meet Long-Range National Needs, Aug ‘10)
Regulatory Science Priorities

2. Leverage existing initiatives or form new partnerships
   – Enhance “data sharing” to standardize models, study endpoints, triggers-to-treat, etc.

3. Expedite licensure review process by engaging cross functional expert teams early
Partnerships to Advance Regulatory Science

• Build on the FDA-NIH Collaboration Initiative (established 2/2010)
  – FDA does not have to invest resources in a research capacity
• Sponsors with USG contracts have regular meetings with the funding agency. FDA scientist present at significant timepoints may improve communication
  – areas to balance: confidentiality, conflict of interest, workloads
• Public-Private
  – Early development partnerships between industry and DoD labs or NIH National/Regional Biodefense Labs
  – Alliance for Biosecurity
Metrics for Success

2 Year Goals

– Finalize Guidance Document for the Animal Rule
– Initiate risk communication strategy to public
– Establish dedicated cross-divisional (or new dedicated division!) review teams to evaluate MCMs under the Animal Rule

5 Year Goal
License 3 MCMs, using the Animal Rule
Discussion