



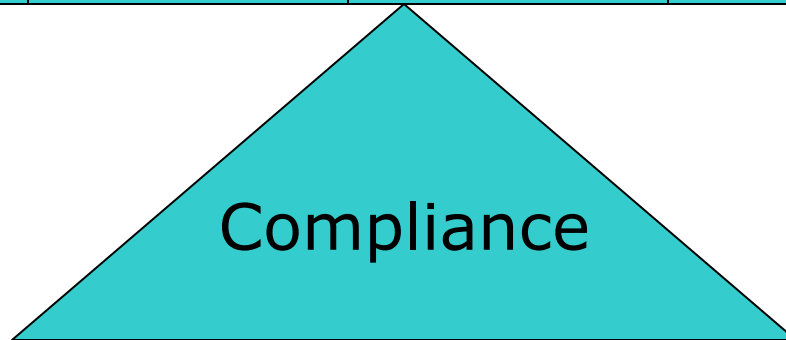
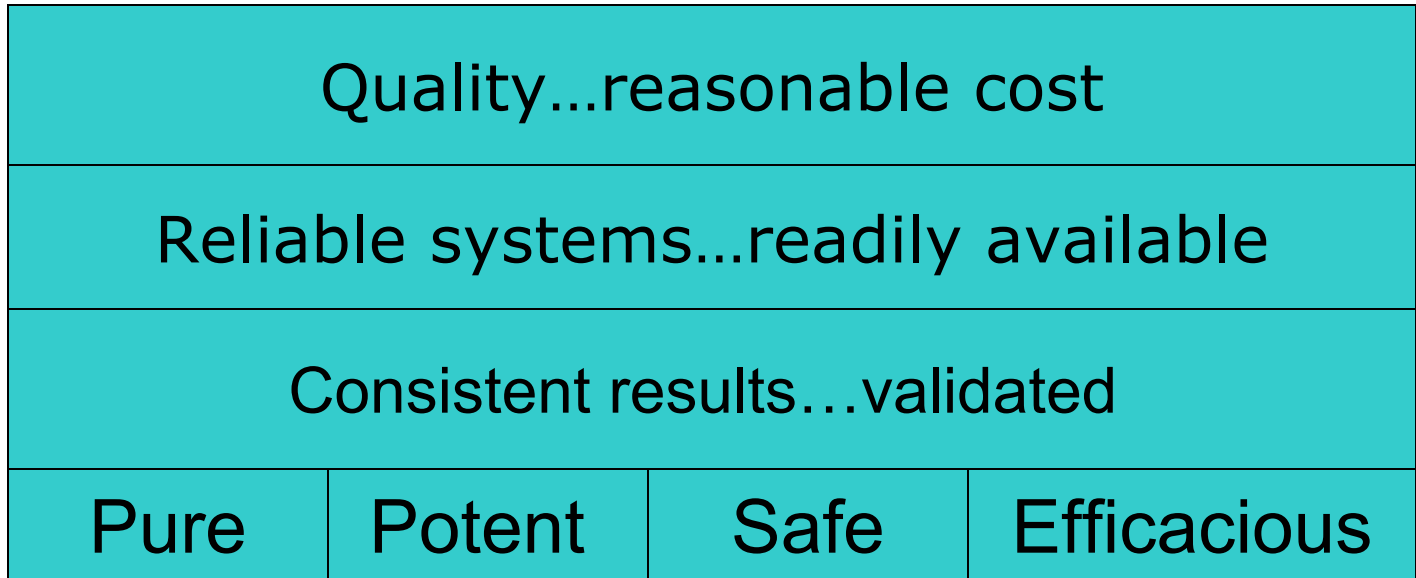
# Reduction, Refinement and Replacement of Animals in Biological Testing

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Animal Health Firm's Perspective  
VBS Public Meeting  
April 6, 2004

# Premise...vaccine potency

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# Compliance.... Title 9 Code of Federal Regulations (9CFR)

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- Virus, Serum, Toxins and Analogous Products: Vectors and Organisms
  - Sets forth the requirements for testing both in laboratory and in animals
- Animal Welfare
  - Sets forth requirements for care and use of animals



# Animal use...compliance and 3-Rs

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- In Biologics, the 3-R's almost exclusively apply to vaccine and challenge treatment of infectious disease
- Potency and animal use...no other data capture method is available or can provide the data output needed
  - No common genetics in all species
  - No common health monitoring
  - Expensive to purchase, hold, and care
  - Slow turn around for data (most species)

# The 3-R's... targets in manufacturing

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- Serial Release and Safety testing
- Requalification of reference reagents
- Pre-license Development (qualification of reagents)
- Post-license Development





# The 3-R's...the industry approach

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- Act now

- Actively use what is available
- Apply as we go forward...constant improvement

- Evolve

- More efficient use of assays
- With technology changes
- Cooperation...academic and regulatory

# Refinement...act now; the IACUC

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- Institutional Animal Care and Use Committee
  - Raises visibility of animal care
  - Ensures veterinarian oversight
  - Enhances infrastructure
    - Daily care, disposition
    - Training

# Refinement...act now; e.knowledge

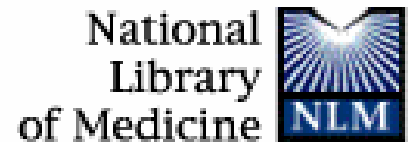
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- Electronic Information Network is being used
  - Firms have IS on site or contracted
  - e.readiness ranges from sophisticated servers to stand alone desk top
  - Enhances communication to multiple sites
  - Removes redundancy in animal use; enhances data use

# Refinement...evolving; enrichment

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- The 3-R's are well published...information is available and being used
- Quick searches for critical information
  - Non-intrusive analgesics and anesthesia
  - Non-invasive data gathering methods on disease and immune response
  - Housing improvements



# Reduction...reduce variance

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- Biometrics
  - Part of the IACUC
  - Fewer studies; right numbers
  - Better clinical readout...less statistical spread
  - Focused clinical readout...fewer variables
- Faster, data review
  - Submission completeness (firms)
  - Turn around (CVB)

# Reduction...evolving; with R&D

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- Enhance stability components/methods
  - Larger serials
  - Fewer safety studies
- Characterize the antigen
  - Use national reference standards
    - differences in vaccine preps, purity, adjuvants
  - Fewer requalifications



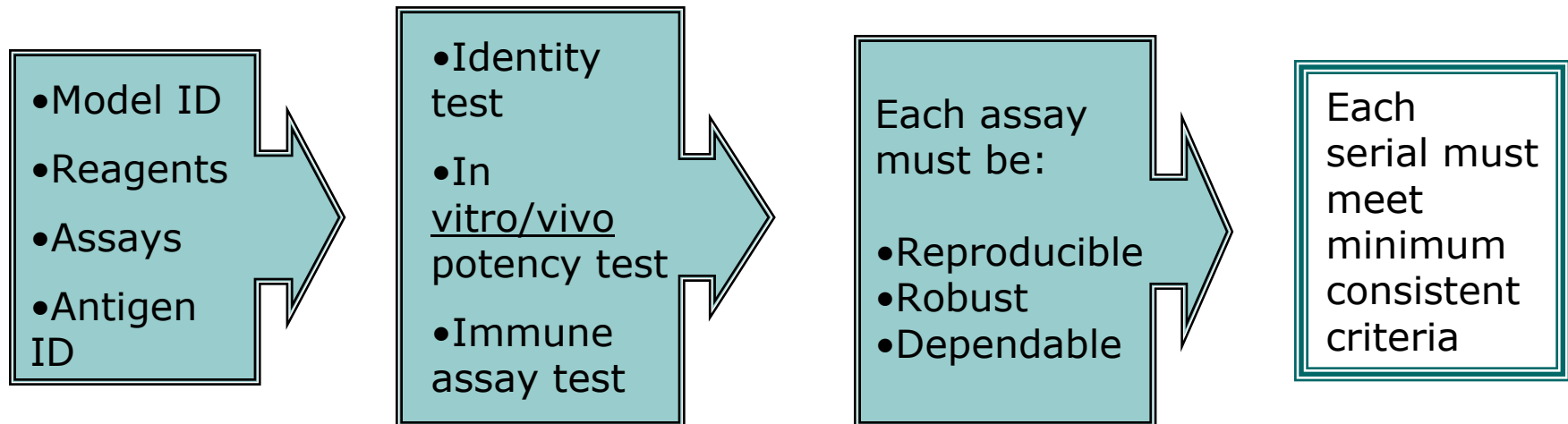
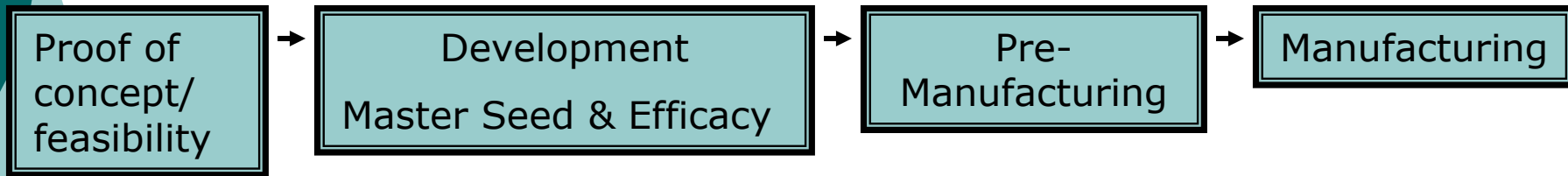


# Replacement...animal to in vitro

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- An absolute target: Induce immunity and challenge without the animal
- Efficient use of what's available: in vitro tests that detect and quantify antigen, and correlate to protection... few tests measure critical immune response function.

# Producing a vaccine...consistency

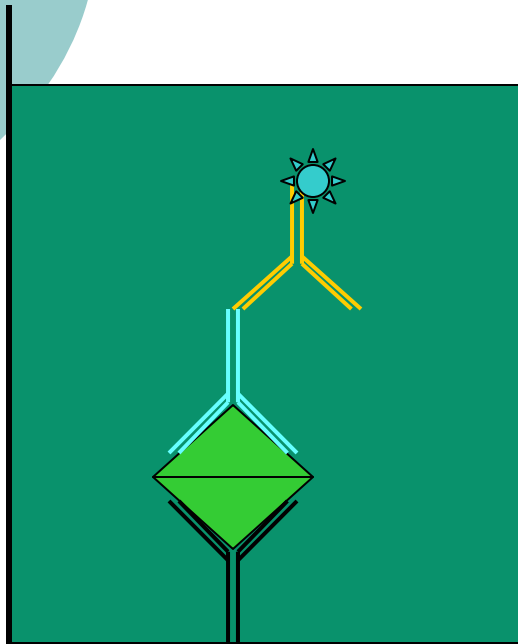


# In vitro potency...workhorse

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Robust

Inexpensive



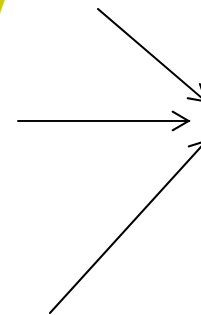
Solid phase (plate)

- Antispecies Conjugated Antibody

- Detector Antibody

- Antigen

- Capture Antibody



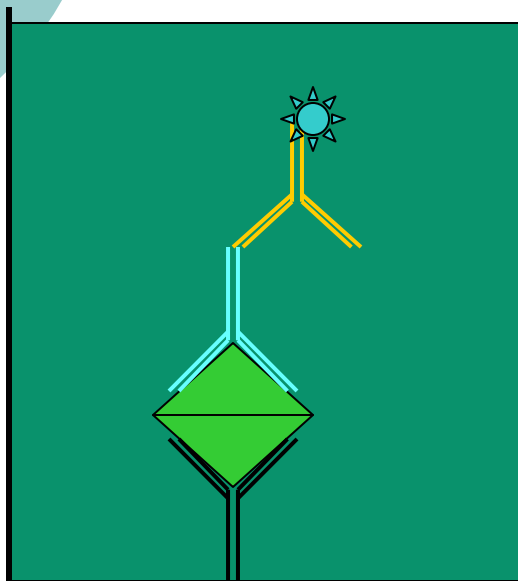
- Minimum use of animals

- Stable

- Can be validated

# In vitro potency...evolving the assay

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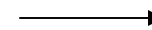
**Solid phase (plate)**

• **Antispecies Conjugated Antibody**

• **Detection Antibody**

• **Antigen**

• **Capture Antibody**



- Biochemical characterization
- Immunological characterization
- Defined production
- Can be validated

# Summary...3-R's for industry

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- Act now...
  - Active IACUCS
  - Effective use of information (e.readiness)
  - Cooperation (Academics, government)
- Evolve...
  - Characterize and validate present systems
  - Incorporate new systems with new products
  - Advance with technology (e.readiness)