Reduction, Refinement and Replacement of Animals in Biological Testing

Animal Health Firm’s Perspective
VBS Public Meeting
April 6, 2004
Premise... vaccine potency

- Quality... reasonable cost
- Reliable systems... readily available
- Consistent results... validated
- Pure
- Potent
- Safe
- Efficacious

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

- **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
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

- 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

- 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

- 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

- 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

- 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

- 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

- 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

- 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

- **Proof of concept/feasibility**
  - Model ID
  - Reagents
  - Assays
  - Antigen ID

- **Development**
  - Master Seed & Efficacy
  - Identity test
  - In vitro/vivo potency test
  - Immune assay test

- **Pre-Manufacturing**
  - Each assay must be:
    - Reproducible
    - Robust
    - Dependable

- **Manufacturing**
  - Each serial must meet minimum consistent criteria
In vitro potency…workhorse

Robust

- Minimum use of animals
- Stable
- Can be validated

Inexpensive

- Antispecies Conjugated Antibody
- Detector Antibody
- Antigen
- Capture Antibody

Solid phase (plate)
In vitro potency...evolving the assay

- Capture Antibody
- Antigen
- Detection Antibody
- Antispecies Conjugated Antibody

Solid phase (plate)

- Biochemical characterization
- Immunological characterization
- Defined production
- Can be validated
Summary...3-R’s for industry

- 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)