FDA-ICCVAM 3Rs

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CDER

- Participant in ICH guidance development:
- International harmonization reduces repetition of studies and reduces animal use in overall drug development
- No acute lethal tox
- Combine endpoints-no stand-alone assays for local tox
- Exposure and dose limits for tox studies
- Exploratory clinical studies section reduces use of animals needed to support clinical studies
- Defer reprotox studies until later in development for biologics

CDER-Phototox

- Use 3T3 photocytox assay instead of animals
- Eliminated any photocarc testing

CDER-Carcinogenicity

- Waive carc studies for most biologics
- Working on criteria for waiving carc for small molecules
- For Impurities: use SAR

CDER-Reprotox

- Considering an alternative (in vitro) battery to sometimes replace one species for regulatory use (already used as screens in drug discovery)
- Considering reuse of animals normally discarded before pre-postnatal studies

CDER Practice

- No need for Draize test for skin or eye (e.g., in vitro/in vitro alternatives-- accept BCOP assay)
- Accept nonanimal pyrogenicity assays (if applicable to product)

CDER ICCVAM Activities

- Contributes to DARPA and NCATS initiatives on “human on a chip” programs
- Supports work on a dermal sensitization nonanimal battery
- Supports work on pathway-based assays
- Supports work on ocular assays for no ocular irritation

CBER- Vaccines (a)

- Continued Leadership in International Efforts to Replace Murine Histamine Sensitization Test HIST for Acellular Pertussis Vaccines
  - Prague meeting. NC3Rs Workshop held in conjunction with the 9th World
  - Congress on Alternatives and Animal Use in the Life Sciences, in Prague. Alternatives to the Murine Histamine Sensitization Test (HIST) for Acellular Pertussis Vaccines: Progress and Challenges in the Replacement of HIST

Vaccines (b)

  - International Multi-laboratory Study of Alternatives to HIST ongoing the summer London meeting to discuss results of Multi-laboratory Study

- Ongoing research on non-animal approaches to potency testing for vaccines such as rabies (with USDA)
- Accept non-animal endotoxin testing if appropriate for product

CBER- Cellular and Gene Therapies

- Publication of Final Guidance for “Preclinical Assessment of Investigational Cellular and Gene Therapy Products”
  - Specific section on alternatives (III.B.8)
  - Product area specific 3R’s approaches
  - http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/ucm376136.htm
- Accept non-animal endotoxin testing if appropriate for product

CFSAN

- Represents FDA on Tox 21
- Contributes to DARPA and NCATS initiatives on “human on a chip” programs
- Supports work on AOPs for As
- Supports work on a dermal sensitization nonanimal battery
- Supports work on ocular assays for no ocular irritation
- Uses QSAR and read across when applicable