So-Called “Blinded” Pathology Slide Evaluation

An iterative process for identification of subtle differences among groups of experimental animals

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"NORMAL"

PATHOLOGICAL HYPERPLASIA AND PRENEOPLASIA

ADENOMA

CARCINOMA

"Morphologic evidence" (drawing by Siné)
“NORMAL”

PROTEIN DROPLETS
TUBULAR BASOPHILIA
LYMPHOID INfiltrates
PROTEIN CASTS
FOCAL MINERALIZATION

NEPHROPATHY

END-STAGE KIDNEY
GOAL = identify differences between groups attributable to treatment
Establish a Baseline
(Define “Normal”)

• What is “normal” in the broad context of toxicologic pathology
• What is “normal” in the context of a specific study
Establish a Baseline
(Define “Normal”)

• What is “normal” in the broad context of toxicologic pathology
  – There is a range of change
  – “Normal” determined by training, published literature, and experience
  – The greater the experience, the broader the range of “normal”
“NORMAL”

PROTEIN DROPLETS
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“NORMAL”

PROTEIN DROPLETS
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Establish a Baseline (Define “Normal”)  

• What is “normal” in the context of a specific study  
  – Strain, age and sex of animal model  
  – Level of magnification used in the microscopic examination  
  – Amount of real estate available for examination  
  – Timeframe for evaluation
Commonly Accepted Practice for Routine Safety Assessment Toxicity Studies

• Evaluate with knowledge of treatment groups
• Go back and do a “blinded” review to sort out subtle details

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Best Practices Guideline: Toxicologic Histopathology

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Biomarker Effort

Define the utility of a new biomarker by anchoring it to a whole animal effect such as organ weight change or morphological change in the target tissues.

To definitively identify a true morphological change, even a subtle change or a NOEL, “blinded” slide evaluation will provide the most accurate and unbiased assessment.
Recommendation

• Establish the baseline of “normal” for the study by examination of target tissues from some or all of the controls
• Establish the upper range of lesion severity by examination of target tissues from some of the highest dose
Recommendation

• Establish the baseline of “normal” for the study by examination of target tissues from some or all of the controls

• Establish the upper range of lesion severity by examination of target tissues from some of the highest dose

• Perform the “blinded” evaluation within a narrow window of time
Recommendation

• Mask slide identification and do a “blinded” evaluation of slides
  – Include some or all of the controls
  – Perform the blinded evaluation within a narrow window of time (e.g., all in one afternoon)
  – For complex constellations of change, it may be necessary to do multiple blind evaluations by focusing on a specific change each time
Trust me. I’m a pathologist!