



**NTP**

National Toxicology Program

# Longitudinal Residual Evaluations for Identifying Uterine Proliferative Lesions

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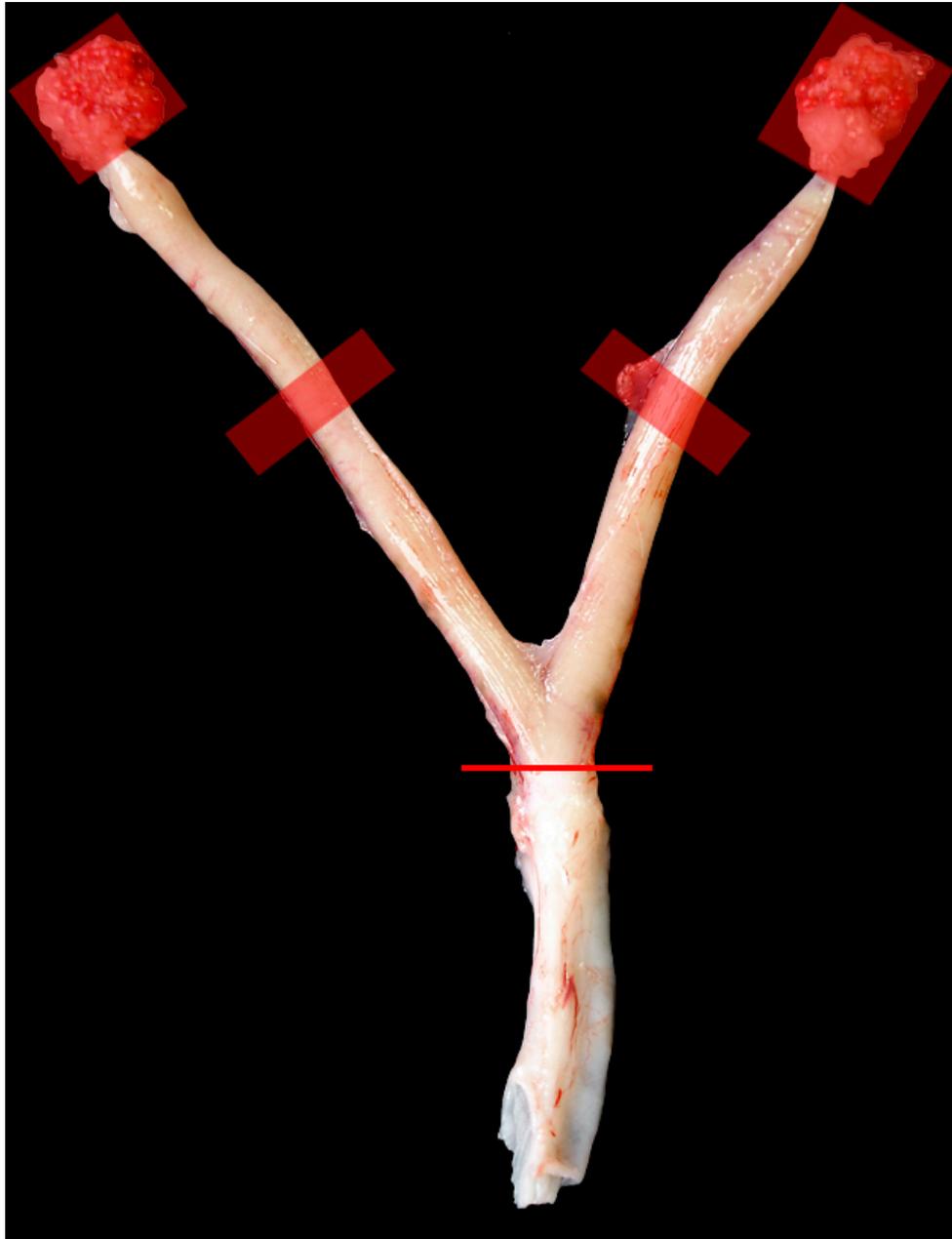


# Current and Prior NTP Studies that have Used the Uterine Longitudinal Sectioning Protocol

- Tetrabromobisphenol A
- Cimstar
- Green Tea Extract
- Indole-3-Carbinol
- DE-71
- 2,3 Butanedione

# Original Transverse Versus Residual Longitudinal Uterine Reviews

- Original transverse tissue review
  - Transverse section through each uterine horn
  - Cervix/vagina not processed, unless gross lesions
- Residual longitudinal tissue review
  - Remaining formalin fixed cervix, vagina, and uterine remnants were sectioned longitudinally
- Original rationale for residual longitudinal tissue review came from the tetrabromobisphenol A study
  - To determine the primary location for adenocarcinomas in the cervix and vagina
  - To review all the cervixes for hyperplasia/fibrosis

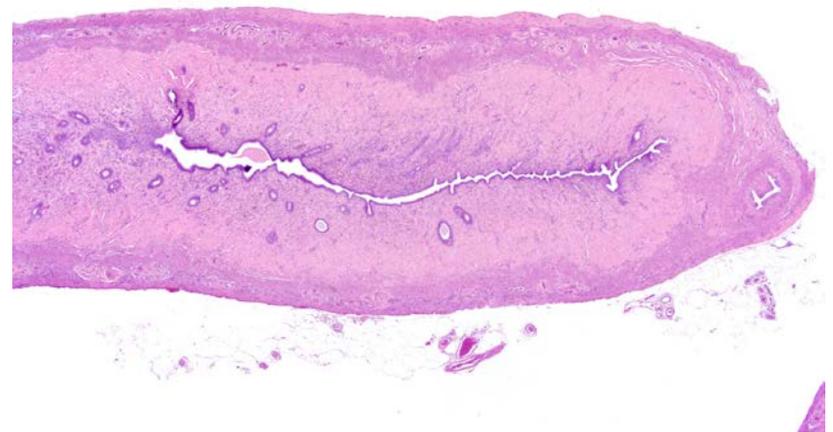
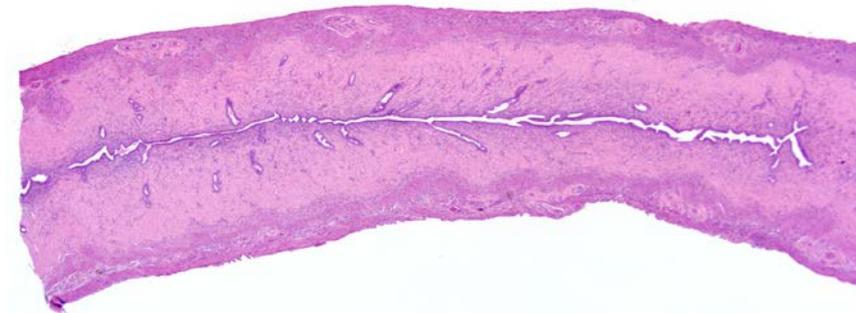


- Gross image of normal female rat reproductive organs
- Ovaries (red boxes) are attached
- Thick red horizontal lines show where a transverse cut is made through the uterine horns in the original review

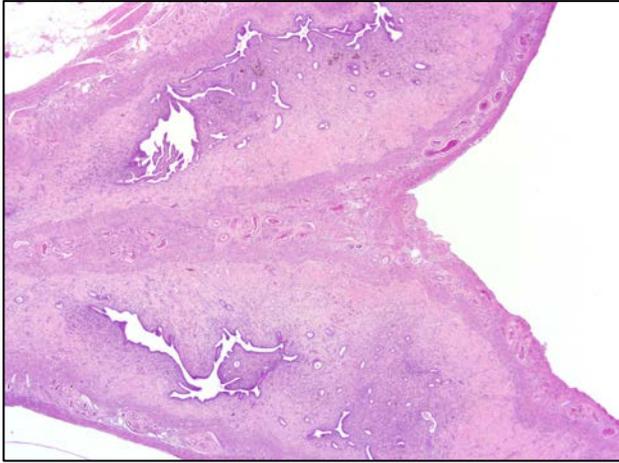
# Original Review: Transverse Section From Each Uterine Horn



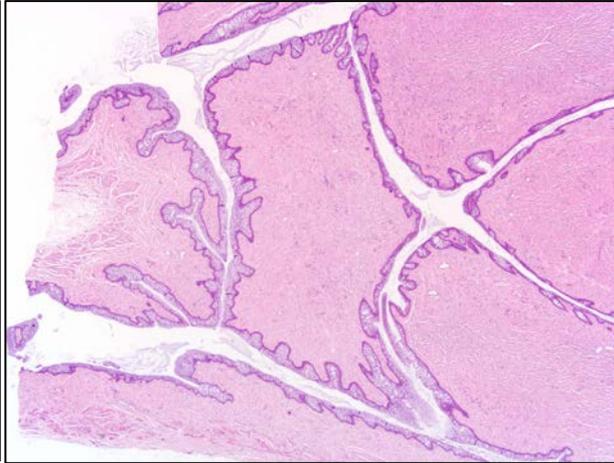
# Longitudinal Sections of Left and Right Uterine Horns



# Additional Sections of Longitudinal Tissue



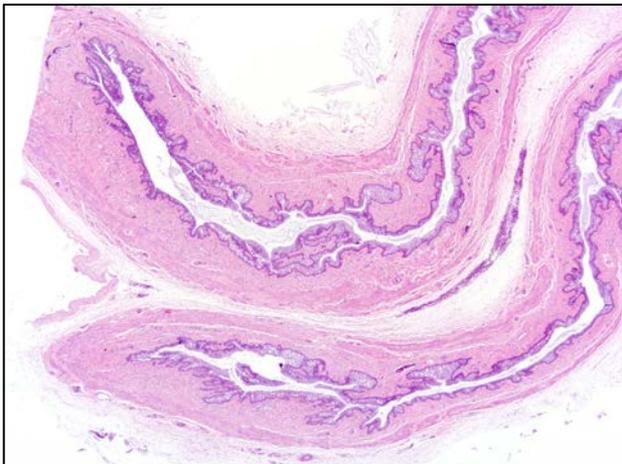
Uterus Body



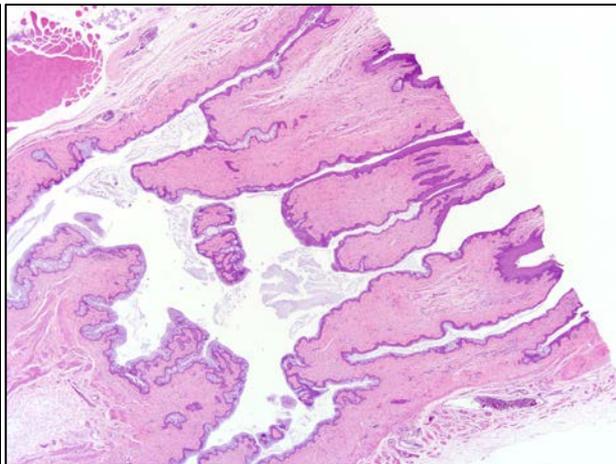
Distal Cervix



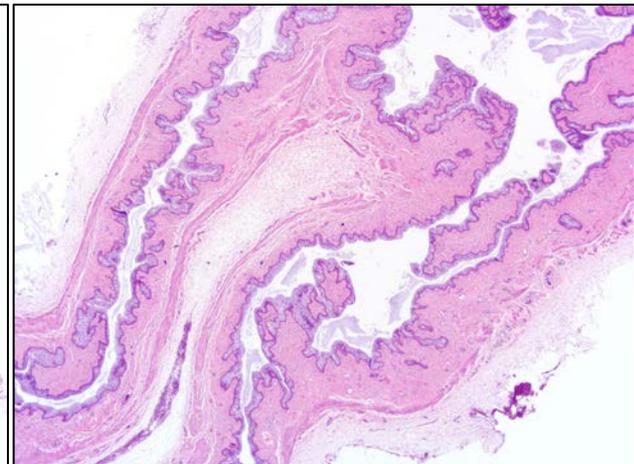
Proximal Cervix



Distal Vagina

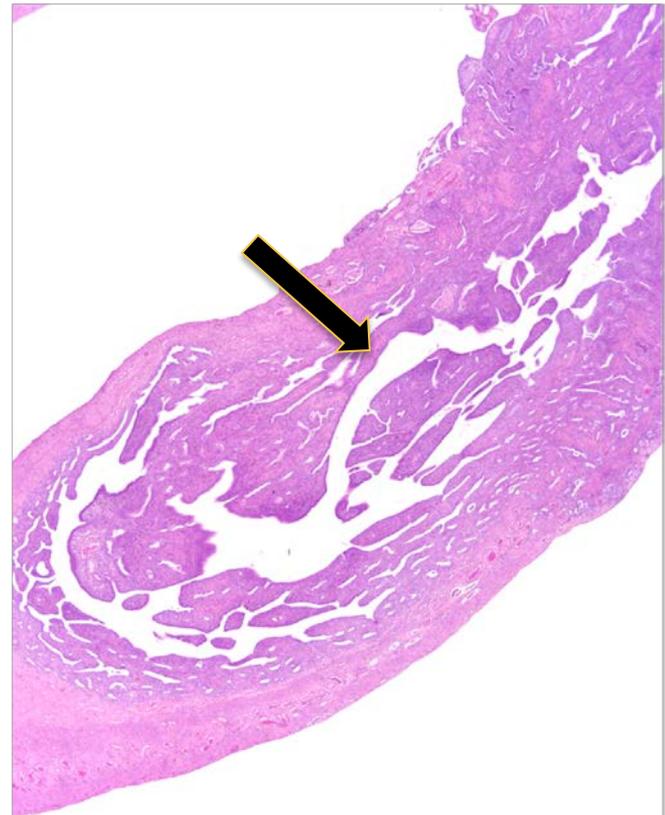
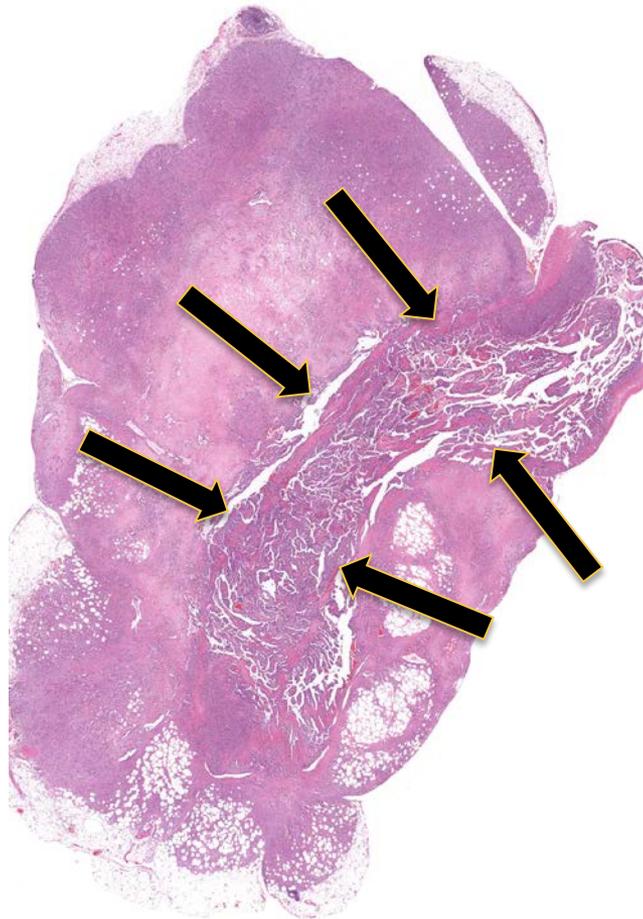


Proximal Vagina



Vagina/Cervix Junction

**Uterus on left shows a large expansive adenocarcinoma that was detected grossly.  
Uterus on right also has an adenocarcinoma, but it was not detected grossly.**



# Tetrabromobisphenol A Study Data

Tumor	0mg/kg	250mg/kg	500mg/kg	1000mg/kg
<b>ORIGINAL TRANSVERSE REVIEW</b>				
Adenoma, Adenocarcinoma, or Malignant Mixed Müllerian Tumor	3**	7	11*	13**
<b>RESIDUAL LONGITUDINAL REVIEW</b>				
Adenoma, Adenocarcinoma, or Malignant Mixed Müllerian Tumor	6**	10	16**	16**
Atypical Hyperplasia	2	13**	11**	13**
<b>COMBINED ORIGINAL TRANSVERSE AND RESIDUAL LONGITUDINAL REVIEWS</b>				
Adenoma, Adenocarcinoma, or Malignant Mixed Müllerian Tumor	6**	11	16**	19**
Atypical Hyperplasia	2	13**	11**	13**

\* Positive trend test or significantly different ( $p \leq .05$ ) from the control group by Poly 3 test

\*\* Positive trend test or significantly different ( $p \leq .01$ ) from the control group by Poly 3 test

# Summary

- Residual longitudinal sectioning
  - Revealed additional uterine tumors, pre-neoplastic lesions, and non-neoplastic lesions in all groups
  - Was not included in the historical control data
  - Provided accurate diagnoses for some non-neoplastic lesions
    - Example: uterine dilatation due to cystic endometrial hyperplasia or uterine polyp
  - Determined primary site of invasive tumors
    - Cervix, vagina, uterus
  - Avoided misinterpretation of gross lesion incidences
    - Example: Cervical lesions
- Has been incorporated as standard protocol for NTP subchronic and chronic studies