



NTP
National Toxicology Program

Contract Concept : Pathology Peer Review and Pathology Support

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NTP Board of Scientific Counselors Meeting
June 25, 2013



Purpose of the contract

- The purposes of the current 3 contracts are to provide independent pathology peer review and pathology services for the tremendous amount of studies conducted by the NTP and NIEHS intramural research.
- The primary objective is to verify and generate accurate data in NTP studies.
- Other objectives include providing staffing, necropsy, histology, special techniques, training, and support for NTP and NIEHS investigations.

NTP studies

- 2-year bioassay - 800 animals and ~ 32,000 tissues
- 90-day study - 240 animals and ~ 10,000 tissues
- Nat'l Center for Toxicological Research (FDA)
- Immunotoxicity studies
- Neurotoxicity
- Multigenerational & modified one generation
- Reproductive and developmental
 - Estrous staging by vaginal cytology
- Genetically Modified Models (GMM)

Near-term expected number of annual studies

5	RACB/DART (Developmental and Reproductive Toxicology studies)
5	MOG (Modified one-generation studies)
10	2-year chronic and/or perinatal (mouse and rat)
20	90-day subchronic (mouse and rat)
15	14-day acute (mouse and rat)
4	NCTR chronic studies
10	other (i.e., aging studies, toxicogenomics, immunotoxicity, neurotoxicity)

NTP pathology review process

- Viewed as international gold standard by agencies such as EPA, FDA, NIOSH, and IARC
- Verifies and establishes consistency in pathology using standardized criteria
- In place for > 30 years
- Comprised of
 - Audit of Pathology Specimens (APS)
 - Pathology Data Review (PDR)
 - Pathology Quality Assessment (PQA)
 - Pathology Working Group (PWG)

Audit of Pathology Specimens (APS)

Review of:

- Slides, blocks and wet tissues (10%)
- Specimen identification
- The quality of documentation
- Physical quality of the materials
- Adherence to the NTP specifications

Pathology Data Review (PDR)

Initial stage of review that defines:

- Target organs
- Unusual findings
- Potential discrepancies
- Consistency in terminology

Quality Assessment (QA)

- Organs to be reviewed for all lesions
- Organs to be reviewed for specific lesions
- Specific lesions for review
- All neoplasms

PWG coordinator responsibilities

- Organs to be reviewed for all lesions
- Organs to be reviewed for specific lesions
- Specific lesions for review
- All neoplasms

Pathology Working Group (PWG)



External Pathologists

PWG Coordinator

Study Pathologist

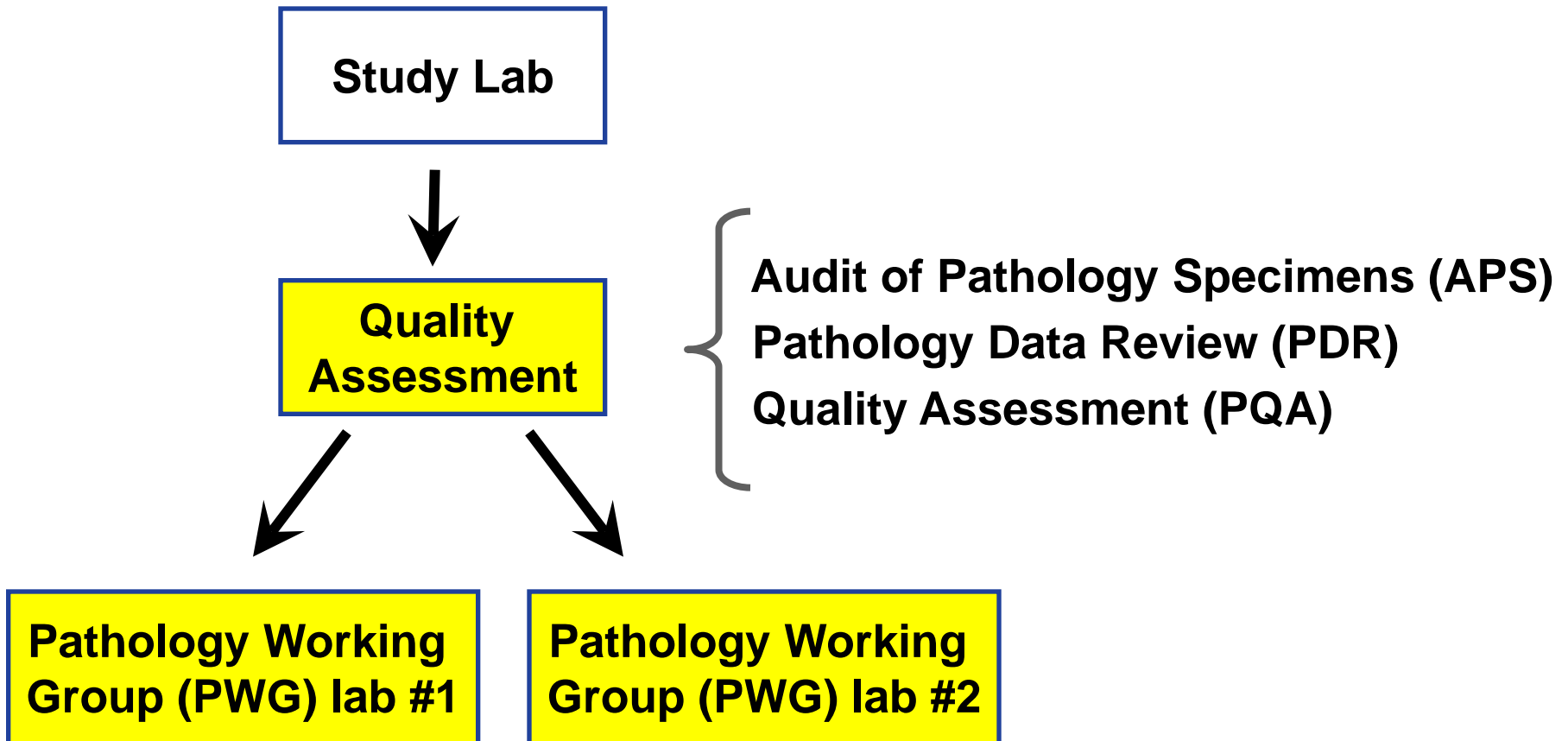
PQA Pathologist

NTP Pathologists

PWG objectives

- Resolve discrepancies
- Confirm diagnoses for potential treatment effects
- Harmonize nomenclature
- Address mechanisms
- Further characterize lesions

Current workflow for NTP pathology peer review



New workflow for NTP pathology peer review

Study Lab



Pathology
Peer Review

- Audit of Pathology Specimens (APS)
- Pathology Data Review (PDR)
- Quality Assessment (PQA)
- Pathology Working Group (PWG)

Benefits of new method

- Provides flexibility
 - multiple labs with same capabilities
 - option to assign a PWG coordinator
- Efficiency (< 12 mos.)
- Cost savings
- Similar to NCTR model
- Maintain high NTP standards

Types of pathology support

- “Phenotyping” animal models
- Histology and histopathology evaluation
- Electron microscopy
- Digital image archives
- Neoplastic and non-neoplastic atlases
- Re-evaluation of tissues - kidney, uterus, or brain
- Assist in arranging topical workshops and retrospective studies

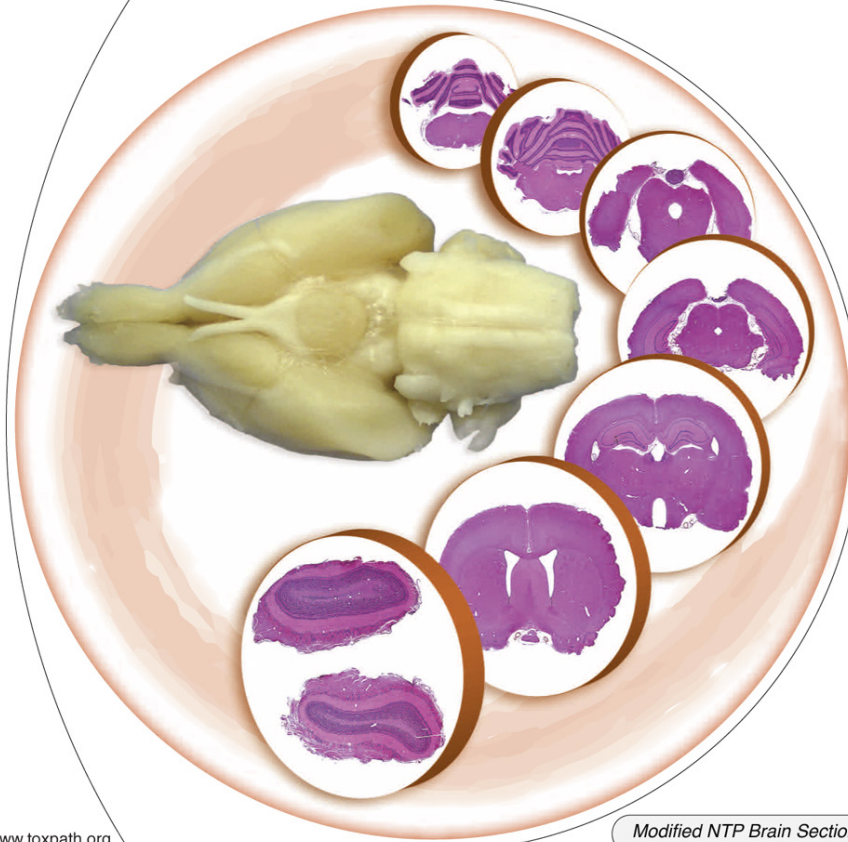
TOXICOLOGIC PATHOLOGY



Volume 39
Number 3
2011

The Official Publication of the Society of Toxicologic Pathology

and the British Society of Toxicological Pathologists



www.toxpath.org
ISSN: 0192-6233

Modified NTP Brain Sectioning



Non-Neoplastic Lesion Atlas

A guide for standardizing terminology in toxicologic pathology for rodents.



Purpose

Guide

Acknowledgements

Contact

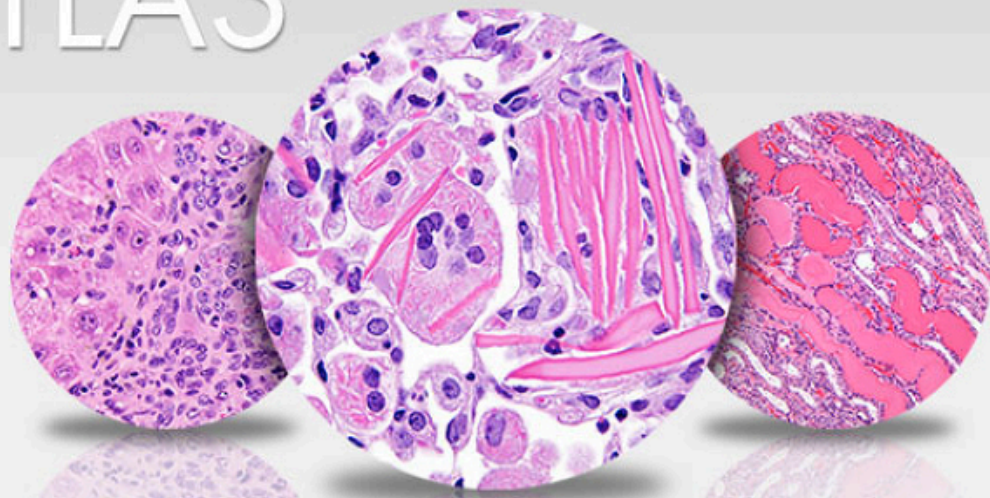
Atlas Home

- ▶ Alimentary
- ▶ Circulatory
- ▶ Endocrine
- ▶ Hematopoetic
- ▶ Integumentary
- ▶ Muscuolskeletal
- ▶ Nervous
- ▶ Reproductive
- ▶ Respiratory
- ▶ Special Senses
- ▶ Urinary

National Toxicology Program

Non-Neoplastic Lesion ATLAS

A guide for standardizing terminology
in toxicologic pathology for rodents.



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Changes made to the current statement of work

- (1) The QA pathologist will also serve as the PWG coordinator and manage the PWG together with the NTP pathologist.
- (2) Conduct of the PWG will be consolidated into the PQA process, thereby streamlining the pathology review process overall and decreasing the time and cost to achieve consensus & final data.
- (3) At the discretion of the NTP and depending on the study, a PWG Coordinator from an independent lab may be assigned to conduct a PWG.



NTP
National Toxicology Program

**Contract Concept :
Pathology Peer Review for DNTP studies
and Pathology Support for DNTP and
DIR projects**





The BSC members are asked to review the concept for overall value and scientific relevance, as well as for fulfilling the program goal of protecting public health.

1. scientific, technical, or program significance of the proposed activity
2. availability of the technology and other resources necessary to achieve required goals
3. extent to which there are identified, practical, scientific, or clinical uses for the anticipated results.
4. where pertinent, adequacy of the methodology to be used in performing the activity

The NTP seeks approval from the BSC to continue this type of activity using a contract mechanism.