

STP Position Paper: Recommended Practices for Sampling and Processing the Nervous System (Brain, Spinal Cord, Nerve, and Eye) during Nonclinical General Toxicity Studies

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Abstract:

The Society of Toxicologic Pathology charged a Nervous System Sampling Working Group with devising recommended practices to routinely screen the central and peripheral nervous systems in Good Laboratory Practice-type nonclinical general toxicity studies. Brains should be trimmed similarly for all animals in a given study and weighed. Certain structures should be sampled regularly: caudate/putamen; cerebellum; cerebral cortex; choroid plexus; eye (with optic nerve); hippocampus; hypothalamus; medulla oblongata; midbrain; nerve; olfactory bulb (for rodents only); pons; spinal cord; and thalamus. Brain regions may be sampled bilaterally in rodents using 6-7 coronal sections, and unilaterally with 6-7 coronal hemi-sections in non-rodents. Spinal cord and nerves should be examined in transverse and longitudinal (or oblique) orientations. Most Working Group members considered immersion fixation in formalin (for CNS or PNS) or a solution containing acetic acid (for eye), paraffin embedding, and initial evaluation limited to hematoxylin and eosin (H&E)-stained sections to be acceptable for routine microscopic evaluation during general toxicity studies; other neurohistological methods may be undertaken if needed to better characterize H&E findings. Initial microscopic analysis should be qualitative and done with foreknowledge of treatments and doses (i.e., "unblinded"). The pathology report should communicate clearly structures that were assessed and methodological details. Since neuropathologic assessment is only one aspect of general toxicity studies, institutions should retain flexibility in customizing their sampling, processing, analytical, and reporting procedures as long as major neural targets are evaluated systematically.