
Guest Editorial

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Pathology Peer Review

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This issue of *Toxicologic Pathology* contains an article by Morton et al. that provides recommendations for pathology peer review of nonclinical studies. This is overall a clear, very detailed, and very well-organized manuscript summarizing current recommended practices by experts in the profession and clearly defines the value that peer review lends to the final diagnostic process in toxicological pathology. Although many articles have provided commentary and recommendation on the evolving role of the peer review in creating quality, credible pathology data, the present article consolidates and expands the preferred pathology peer review practices. It is anticipated that pathology peer review will continue to evolve, and this article documents the state of the art at the present time.

Assessment of human risk from exposure to a chemical or test material involves evaluation of multiple factors, including potential exposure scenarios, toxicokinetics, and ability to manage risk by controlling exposure/dose. A cornerstone for making risk-based determinations for safety of a compound relies on evaluation of gross, microscopic, and clinical pathology in rodents and other laboratory animal species after exposure to the test material of concern. These animal studies require the pathology data to be of the highest quality with confidence in the final diagnoses in order to provide a biological basis for determining potential risk to humans who may be accidentally or intentionally exposed to the compound or test agent. Given that the pathology evaluation is based on training and judgment gained from years of experience, a well-defined peer review process can assist the study pathologist in providing the most accurate data for interpretation, which, in turn, provides the biological basis for characterization of potential human risk.

The discipline and art of pathology has, historically, been one in which pathology practitioners have learned from those more experienced and has required constant review, re-evaluation, and continual learning throughout the career of the pathologist. Furthermore, each pathologist may develop specialized expertise in one or more species, one or more organs or tissues, or lesions produced by one or more classes of compounds, as well as expertise in special techniques such as immunohistochemistry, genomics, and ultrastructural examination, for example. The peer review pathologist may often have areas of expertise or experience in pathology that are different from those of the study pathologist and, therefore, may provide additional insight to help in interpretation of unfamiliar lesions, techniques, and animal models used in toxicity studies.

The recommendations presented in this issue of *Toxicologic Pathology* are an excellent example of this heritage in pathology. They present the state of the art, a thorough description of appropriate methods in performing a peer review, and a clear statement of the goal of the review process. The primary goal of the pathology peer review is to help ensure an accurate reporting of the spectrum of test article-related lesions that occurred in the study. It is not designed to catalog a list of discrepancies, focus on incidental/trivial findings, or grade the quality of the pathologist. Although those issues may become relevant in the review of a study, the purpose of the peer review process is to ensure the pathology report is an accurate reflection of the pathology findings for the study. The approach for the peer review as described in these recommendations is consistent with that goal.

As an increasing number of studies are conducted by contract research organizations, some of the peer reviews that took place informally at the sponsor's facility are now conducted by a sponsor-designated, peer review pathologist. This pathologist may often provide an additional, valuable perspective on the study, as the sponsor pathologist is often familiar with known (unique) mechanisms of action of the test article and aware

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of test article effects that may have occurred at higher doses in range-finding studies or in other species and is familiar with terminology used in other studies in support of the test article. The peer review pathologist helps to ensure that all relevant, subtle test article-related lesions are identified and characterized and that terminology and grading are consistent across studies. As noted in the article by Morton et al., safety for patients/participants in clinical trials is a primary goal of the sponsor in the conduct of these studies, and a thorough and accurate evaluation of all preclinical data, including the pathology results, though a peer review process is critical to this effort.

A signed peer review memo, which indicates a peer review was conducted verifies the process and outlines how discrepancies were resolved, should be included with the study report. Studies submitted with documentation of a peer review may provide greater confidence to regulatory agencies as to the quality/accuracy of the results compared to a study in which a peer review was not performed.

The authors note that a review of a subset of control animals should not be required by default but should be based on the discretion of the peer review pathologist. The authors of this commentary would suggest that a review of all organs including appropriate sampling of control animals is useful for determining the incidence of spontaneous background lesions and overall quality of the animals used in the study. It may not be considered necessary in all cases when several studies from the same laboratory during a similar time period are being

reviewed. We encourage peer review pathologists to consider evaluation of all tissues from a subset of control animals, as appropriate, as an important adjunct to improving the historical control database and for the optimal evaluation of each study (Keenan et al. [2009]. *Toxicol Pathol* **37**, 679–93).

Publication of an article is one of the first steps in the scientific process. Publication is followed by evaluation, discussion, and subsequent publications that may confirm, modify, or alter the findings of the original publication. Thus, these recommendations should be considered as current guidelines for the practice of pathology peer review, and the manuscript should be regarded as a “living document” for subsequent discussion and continued refinement. It is our opinion that the article by Morton et al. is a significant step in documenting the current practices for pathology peer review. Publication of this article has the added bonus of stimulating additional discussion as the toxicologic pathology community continues to examine the best procedures for providing quality pathology data for nonclinical studies. The authors are to be commended for their extensive discussion and incorporation of ideas from the toxicologic pathology community that has led to the endorsement of the approach by the Society of Toxicologic Pathology, the European Society of Toxicologic Pathology, the Japanese Society of Toxicologic Pathology, the British Society of Toxicologic Pathology, the French Society of Toxicologic Pathology, the Italian Society of Toxicologic and Experimental Pathology, and the Society of Toxicologic Pathology–India.

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