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Society of Toxicologic Pathology Position on Histopathology Data Collection and Audit Trail: Compliance with 21 CFR Parts 58 and 11

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ABSTRACT

The purpose of this paper is to discuss the requirement of the audit trail to track changes made to the histopathology data, in order to be compliant with the Code of Federal Regulations (CFR), Volume 21, for both Part 58 (Good Laboratory Practices [GLP]) and Part 11 (Electronic Records/Signatures).

Keywords. 21 CFR; histopathology; audit; electronic signature.

Raw data is defined (21 CFR Part 58) as any record (laboratory worksheet, memoranda, or note) that results from an original observation or activity in a nonclinical laboratory study that is necessary for the reconstruction and evaluation of the report of that study. However, there has been a longstanding consensus with the U.S. Food and Drug Administration (FDA) that for purposes of compliance with GLP, the histopathology raw data is the signed and dated report from the pathologist. In the preamble to the GLP Regulations, as amended on September 4, 1987, and published in the Federal Register (Volume 52, No. 172, pages 33768–33782), the “pathologists interim notes, therefore, which are subject to frequent changes as the pathologist refines the diagnosis, are not raw data because they do not contribute to study reconstruction. Accordingly, only the signed and dated final report of the pathologist comprises raw data respecting the histopathological evaluation of tissue specimens.” Histopathology observations are considered differently from other observations because they are based on examination of histopathology slides that are durable and can be reevaluated during the conduct of the study and into the future. Also, during the course of a study, the pathologist considers histopathology observations in other tissues and in other animals, as well as other types of data from the study, in developing the final interpretation and diagnoses. Therefore, the initial histopathology observations, based on evaluation of the tissue(s) present on single glass histopathology slides, represent “working interim notes” and these interim notes do not represent raw data.

The Part 11 (Electronic Records/Signatures) regulations were passed to assure that systems and procedures were in place that would ensure the integrity of the electronic records,

and to prevent the falsification of the electronic records. In the GLP-compliant histopathology data collection computer systems used today, a variety of security measures have been incorporated to ensure data integrity throughout the process of histopathology data collection and reporting. These security controls include: limited user access, single and/or multiple password requirements, procedural controls and technical controls built into the systems. A critical point of CFR Part 11 is the requirement of an audit trail for any change to the data. The audit trail will require recording: Who is making the change; When the change is made; What data was changed; and Why the data was changed.

For the histopathology data, the Part 11-specified audit trail should become active after the pathologist has completed the tissue evaluation, finalized the diagnoses and locked the histopathology database. As stated in the preamble to GLP, the Sept. 4, 1987 final rule (Federal Register: Vol. 52, No. 172, pages 33768–33782), “Although the notes taken by a pathologist during histopathological examinations of slides are indeed the results of original observations, these notes are not necessary for the reconstruction and evaluation of the final report.” Therefore, it is not necessary to have an audit trail to track changes to interim notes/records which are not raw data and do not need to be retained. The signed and dated report from the pathologist and the GLP-specified retained specimens (tissue blocks and glass slides) allow for the reconstruction and evaluation of the final report.

In summary, the GLP-compliant electronic histopathology data collection computer systems have security measures incorporated into them to protect the integrity of the data throughout the entire data collection and reporting

processes. In addition, once the histopathology database is locked/completed, an audit trail is activated to track any subsequent changes made. Since the initial histopathology observations/interim notes are not raw data, are not required for study reconstruction and evaluation of the final report,

and are not required to be retained; no audit trail is required to track changes to these interim histopathology notes. Once the histopathology database is locked, a full audit trail entry (who, when, what, and why) is required for each change to the database.