

---

# Regulatory Forum

---

*Toxicologic Pathology*, 35:450–455, 2007  
Copyright © by the Society of Toxicologic Pathology  
ISSN: 0192-6233 print / 1533-1601 online  
DOI: 10.1080/01926230701284509

## Society of Toxicologic Pathology Position Paper on Pathology Image Data: Compliance with 21 CFR Parts 58 and 11

DARRELL L. TUOMARI,<sup>1</sup> RAMON K. KEMP,<sup>2</sup> RANI SELLERS,<sup>3</sup> JOHN T. YARRINGTON,<sup>4</sup> FRANK J. GEOLY,<sup>5</sup>  
XAVIER L. M. FOUILLET,<sup>6</sup> NOEL DYBDAL, RICK PERRY<sup>8</sup>, AND PHIL LONG<sup>4</sup>

<sup>1</sup>*Schering-Plough Research Institute, Lafayette, NJ 07848, USA*

<sup>2</sup>*Merck Research Laboratories, West Point, PA 19486, USA*

<sup>3</sup>*Albert Einstein College of Medicine, Bronx, NY 10461, USA*

<sup>4</sup>*Vet Path Services Inc., Mason, OH 45040, USA*

<sup>5</sup>*Pfizer, Inc., Groton, CT 06340, USA; 5Philip H. Long, Vet Path Services, Inc., Mason, OH 45040, USA*

<sup>6</sup>*Bracco Research SA, Geneva, CH-1228, Switzerland*

<sup>7</sup>*Genentech, Inc., South San Francisco, CA 94080, USA*

<sup>8</sup>*Wyeth Research, Chazy, NY 12921, USA*

### ABSTRACT

The Society of Toxicologic Pathology (STP) has developed the following recommendations for the use of pathology images in compliance with the Code of Federal Regulations (CFR), Volume 21, Part 58 (Good Laboratory Practices [GLP]) and Part 11 (Electronic Records/Signatures). These recommendations include: (1) based on current technologies and practices, pathology images (printed, electronic, or digital) used for data generation (e.g., to make a diagnosis or for morphometric analysis) are raw data that must be authenticated and archived; (2) authentication of an image may be done either by initialing and dating a print of the image or by specifically annotating the electronic image file in compliance with Part 11 regulations; (3) images used for raw data are subject to GLP procedures and controls in order to ensure data integrity including written Standard Operating Procedures, testing/validation of equipment, training of personnel, etc.; (4) validation and/or performance qualification of imaging systems used to support GLP studies must be documented and any exceptions to full validation/qualification must be described in the GLP Compliance Statement for the study; (5) images that are not used for data generation are illustrative images, are not raw data, and generally do not have to be archived; (6) illustrative images should not be used to re-evaluate or supersede the pathologist's diagnosis.

### 1. INTRODUCTION

The use of film and digital imaging technologies is an increasingly important component of the practice of toxicologic pathology in nonclinical studies. The Society of Toxicologic Pathology convened a subcommittee to evaluate the role and use of pathology images in data generation in nonclinical studies and to develop recommendations that ensure their use is compliant with the Code of Federal Regulations (CFR), Volume 21, Part 58 (Good Laboratory Practices [GLP]) and Part 11 (Electronic Records/Signatures). This position paper addresses five main topics:

1. The appropriate rules for acquiring pathology images to be employed in data generation (which become “raw data” at the time they are used to make diagnoses or measurements).

2. The procedural controls that must be in place to protect the integrity of raw data.
3. How images are authenticated (annotated that the image was used for data generation) and archived.
4. Determination of the fate of illustrative pathology images not used for data generation, which are not raw data and generally do not have to be archived.
5. The role and limitations of images during the pathologic evaluation and peer review.

### 2. PATHOLOGY IMAGES USED FOR DATA GENERATION ARE RAW DATA

The GLP regulations, 21 CFR Part 58, Section 58.3 (k), state that raw data:

“may include photographs, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations and recorded data from automated instruments.”

Pathology images may be acquired from gross lesions, slide-based specimens (e.g., tissue sections for

---

Address correspondence to Sue Pitsch, Society of Toxicologic Pathology, 1821 Michael Faraday Drive, Suite 300, Reston, VA 20190, USA; e-mail: spitsch@toxpath.org

histopathological evaluation, dispersed cells for cytology examination, etc.) or from other materials used to support the pathology evaluation (e.g., images generated using a variety of noninvasive imaging technologies, or derived from molecular biology gels, electrophysiology evaluations, etc.). Based on current technology and practices, pathology images become raw data when used for data generation regardless of whether the image was captured and/or stored on film, or electronically or digitally on magnetic or optical media.

Pathology images are used for data generation in two ways: (1) the image is used by the pathologist as the basis of a diagnosis (e.g., electron micrographs), and (2) the image is used to measure the size and/or number of a particular structure (e.g., morphometric analysis). Any pathology image (whether from film or electronic media) that is used for data generation must be authenticated (annotated as raw data) and archived.

As with other data in a nonclinical study, procedures and controls need to be in place to protect the integrity of the image raw data. These procedures and controls are described next.

### 3. PROTECTING THE INTEGRITY OF THE RAW DATA

#### *Written Standard Operating Procedures (SOPs)*

Unless specifically described in the study protocol, written SOPs must describe methods of image data capture and labeling, personnel training, equipment testing and calibration, and image archiving procedures. In instances where images are needed for the interpretation of the study, the Quality Assurance Unit may audit the processes during data generation.

#### *Image Labeling*

Image labeling is the process of ensuring that the image raw data is properly identified. Image labeling is easy when the appropriate label can be placed within the field of view so that the label is captured as part of the image. However, this usually is not possible for photographs taken of cytologic, histopathologic or electron microscopic specimens. Therefore, procedures must be in place to ensure that the appropriate label information (e.g., study number, animal number, sex, dose group or level, specimen identification, magnification, special stains, and date) can be linked back to the raw data images.

For film images, this documentation requires accurate photography log records. Once an image has been printed, the label information should be transcribed onto the image prints. For electronic images, the label information is entered into an electronic file (e.g., metadata) that is linked to the image file. Thus, the image capture SOPs should detail the method by which the appropriate image label information will be recorded at the time of image capture and how this will be transcribed onto the image raw data prints or linked to the image raw data files.

#### *Computer System Calibration and Validation*

Most imaging computer systems are not designed specifically for GLP-compliant pathology applications. Consequently, full GLP-compliant computer system validation of complex imaging technologies may not be possible in a timely manner. Computerized imaging systems should be validated to the extent possible to ensure Part 11-compliance. When full validation is not feasible, the systems should be

tested and/or calibrated to demonstrate that they are appropriate for the intended use. This validation testing must be documented.

When a computerized imaging technology that cannot be fully validated is used for data generation, then the gaps in validation should be described as an exception in the GLP Compliance Statement for the study. Computer systems that lack full audit trail capability may not be able to reliably archive the electronic image files: prints may be the easiest and most reliable method for archiving these images. Lack of full validation should not preclude the use of these important new technologies.

#### *Electronically Generated Images from New Technologies*

A variety of new imaging technologies can be important tools to detect, document, and/or investigate test article-related findings. These technologies create images using highly sophisticated imaging devices that may measure differences in absorption, generation, or transmission of electromagnetic radiation or other energy by a specimen. Examples of such technologies include magnetic resonance imaging (MRI), computerized tomography (CT), dual-energy x-ray absorptiometry (DEXA), positron emission tomography (PET), and ultrasound imaging. These images may be integral to a morphological diagnosis or contribute to a diverse array of data, such as measurements of neural structures in the brain on an MRI scan, measurements of blood flow rates from PET scans, or bone density measurements from DEXA scans. Repeatability of images generated by these technologies, which are often from dynamic living systems, is rarely possible. If these electronic images are used for data generation, then they are image raw data that must be authenticated and archived.

Images may be archived either as authenticated image prints or as an authenticated Part 11-compliant electronic record. Archiving electronic data files for retrieval at a future date is a significant issue, as the computer systems used to create, analyze and review this data are rapidly evolving, and systems rapidly become obsolete. Over time it will become increasingly difficult to maintain these older computer systems and keep personnel qualified to operate them.

This issue was recognized in the February 2003 draft Part 11 guidelines that permit electronic records to be archived to microfiche. Therefore, at some future date, image records originally archived as electronic files may subsequently be converted to prints, which are then annotated and archived. However, if the data generation was based on an image that cannot readily be printed out, one has no option other than to maintain a Part 11-compliant electronic record for the duration required by the GLP (e.g., up to 5 years after study submission).

The use of these technologies can generate a very large amount of electronic data and very large image data files. For example during an MRI scan a large file composed of thousands of different potential views or slices of a specimen can be generated. In such a case, only the images used for data generation must be authenticated and archived. Images that were not evaluated, did not contribute to data generation, and had no impact on the interpretation or integrity of the study (i.e., images that are not raw data) do not need to be annotated and archived. However, when using Part 11-compliant

system for electronic records, it may sometimes be easier to archive the entire electronic file of all the images rather than selectively archive only the images used for data generation.

#### *Morphometric Analysis of Images*

Data generation using morphometric analysis can be performed on a variety of gross, histopathologic/cytologic, or ultrastructural images. Morphometric analysis can be done in a variety of ways, ranging from entirely manual to fully automated procedures. Morphometric analysis of microscopic findings may be performed using the actual slide-based specimen (a real-time image of that tissue or cell preparation) or on a captured image of the specimen. Some analysis programs can manipulate the image (e.g., alter contrast and/or allow for use of size or shape criteria, and/or add pseudo-color as part of their analysis).

Part 11-compliant morphometric analysis systems are able to automatically track all of the manipulations made to an image. Generally, once the image is captured it is stored as an "unalterable archive" file. A Part-11 compliant analytical computer program should track and record all of the manipulations of the electronic image, and this record can be archived as part of the electronic data associated with the image. If the image analysis program cannot automatically track all of the changes made to the image, then an image print of the final manipulated image (e.g., contrast changes, coloring nuclei, etc.) actually used for data generation must be authenticated and archived with the study.

It is important to note that for morphometric analysis of printed or digital pathology images from slide-based specimens, it is not enough to archive the slide-based specimen because the data generation was actually based on the image, not the slide. The cells or tissues on the glass slide are retained as GLP-specified retained specimens (21 CFR Part 58, Section 58.190[a]); the slides are not raw data.

#### 4. IMAGE AUTHENTICATION: FILM VERSUS DIGITAL IMAGES

Image authentication is a procedure by which an image (electronic or print) is specifically annotated to indicate that it was used for data generation, by whom and when (initials and date), at the time of data generation, to certify that the image is authentic for purposes of archiving it as raw data. Image authentication may be either manual (permanent ink on an image print) or electronic annotation to an image record. The authenticated image will be used to verify the accuracy of all future copies of the image. Due to the diversity of images that can be used as raw data, the process of image authentication is illustrated below using a variety of scenarios.

If diagnosis or analysis was performed using a printed image, the most authentic image to archive is the actual photograph used for the analysis so that at any future date, this image can be used to reconstruct the data generation process. This photograph would be authenticated by annotating that it was used for data generation, signing (initialing) and dating at the time of data generation. When film photography is used, the print used for data generation is more appropriate for authentication than the film negative since the print was used for data generation and is the most readable form to the human eye (film negative being the negative image). In general, the film negative is usually archived along with the

photographic print because the film negative facilitates making copies of the print. The film negative may contain images that were not used for data generation that do not have to be archived. However, it is often easier and more convenient to archive the whole film negative, with some superfluous images, rather than to specifically excise them out.

In contrast to film images, there are two options for authentication of a digital or electronic image: (1) an image can be printed and manually authenticated or (2) the electronic record of the image can be authenticated in a Part 11-compliant system.

The use of authenticated image prints is equally valid in digital/electronic photography and film photography. At the time of data collection, the image is printed and then authenticated as described above for printed images. This procedure must be followed when an electronic image file is not Part 11 compliant (e.g., the image software does not have full annotation and audit trail capabilities). In this case, the electronic image may be archived with the annotated print to facilitate making future copies of the image (analogous to archiving the film negative, with the electronic image serving as the "negative"), but the print would be the raw data. Any future printouts of the electronic image file would then be compared to the authenticated print to verify their accuracy.

When an electronic record is used as the image raw data a specific annotation is included in the electronic record file to indicate that the image was used for data generation, by whom and when. Importantly, the electronic record must comply with Part 11 regulations to ensure the accuracy and integrity of the archived image electronic records. Extensive documentation of the testing and procedural controls for all components of the image capture and image data handling systems is necessary for full GLP- and Part 11-compliance. This documentation would include written test scripts to evaluate and verify that various computer program functionalities are working properly and full audit trail for every change made to the data.

In addition, there should be limited access to these data files as part of computer security. Obviously, the procedural controls would be widely different if one were using a camera that recorded directly into a network computer system versus a camera that recorded to a CD versus a camera that recorded to a removable memory card. Electronic image files stored on memory cards can easily be read and manipulated by a wide variety of commercial software. Thus, if the camera recorded the image onto a memory card, specific procedures and chain of custody documentation must be in place to ensure that the images in the camera or memory card are not altered or manipulated prior to the electronic record being placed into a fully Part 11-compliant computer system.

#### *Virtual Slides*

A virtual slide is made using a computer system that scans the entire slide-based specimen slide at high magnification and stores all image data in a large electronic file system. Using this technology and a monitor, the pathologist can move to various areas of the image and examine them at a variety of magnifications. These systems create an electronic copy of a pathology specimen (the cells or tissue section on the glass slide), but a virtual slide cannot be readily printed out.

Consequently, based on current practices and technologies, when a virtual slide is used for data generation, the electronic record must be authenticated at the time of data generation, and then archived in compliance with Part 11 regulations for electronic records. However, there is great potential for new capabilities in the rapidly evolving electronic imaging arena. Advances in software, hardware and automation, could make it possible to reliably recreate an exact image from durable slide based specimens at any future date desired. Thus, archiving of these virtual slides would not be necessary because exact images could be reliably be recreated from the original durable specimens. However, until electronic image systems of this caliber are developed and validated, all virtual slides used for data generation (including those from durable specimens) need to be authenticated and archived.

#### 5. ILLUSTRATIVE IMAGES ARE NOT RAW DATA

In contrast to pathology “raw data” images that are used for data generation (e.g., the basis of a morphologic diagnosis or measurement), illustrative images are captured to exemplify a particular gross or microscopic finding that has already been observed. The purpose of illustrative images is only to convey information about a particular diagnosis or finding; they are not the basis for that diagnosis or finding. Therefore, illustrative images are not raw data because they were not used for data generation; no diagnoses, measurements or interpretations were based on them. A decision to capture illustrative images has no impact on the integrity or interpretation of the study data because illustrative images are not part of the raw data for a study. Illustrative images may be captured and used for a variety of reasons. Several examples are provided in the following discussion.

##### *Illustrative Images for Multi-Company Collaborative Nomenclature Efforts*

When multiple companies/academic institutions/regulatory agencies are involved in sharing illustrative images as part of a nomenclature/diagnostic criteria harmonization effort, study-related information is intentionally omitted from the image labeling. In addition, it is not possible to have standardized training of personnel or calibration/validation of the various computer systems that will be used to view these illustrative images. Often the discussion about these images is not what the diagnosis is, but rather whether or not the image adequately illustrates the diagnostic criteria of interest. These illustrative images may be captured from past or ongoing studies. These illustrative images are not required to be archived with the study.

##### *Protocol-Required Illustrative Images*

Protocols for some studies, such as injection site irritation studies, medical device studies, or wound healing studies, may specify that gross, microscopic, or ultrastructural photographs are taken from some or all animals. As with all other protocol-driven activities, appropriate procedural controls, equipment validation and/or calibration, labeling, and personnel training requirements (as previously described for raw data images) apply to these protocol-driven illustrative images. However, these images are not raw data since they were not used for data generation. These illustrative images are documentation that the protocol-required photography

was done, and archiving of some of these images is performed as specified in the study protocol and/or applicable SOP's.

##### *Illustrative Images Included in the Final Report*

The typical pathology report does not include images. However illustrative pathology images may be included in the pathology report as a tool to convey information or promote a better understanding of the findings observed in the study to the reader of the report. Whenever illustrative pathology images are included in the final report, they will be automatically archived with the study because the final report of the study must be archived (GLP regulations, 21 CFR Part 58, Section 58.190). These illustrative images must be properly labeled to facilitate auditing of the final study report and archiving of the images.

##### *Illustrative Images Submitted in a Regulatory Response*

Following submission of a study report to regulatory agencies, an agency may request more information or clarification regarding pathology findings or specifically request some pathology photographs (which usually concern a change observed histopathologic/cytologic slides). Thus, illustrative images may be included in regulatory responses. The illustrative images in a regulatory response are not required to be archived, but they usually are archived for convenience, as they may be useful in future responses to other regulatory agencies. Since these images are illustrative (not raw data), there is no need to amend the final study report to address the capture and submission of these illustrative images because no new data were generated.

#### 6. ROLE AND LIMITATIONS OF IMAGES IN THE PATHOLOGIC EVALUATION

##### *Gross Pathologic Tissue Evaluation*

In general for the gross pathologic tissue evaluation, the raw data are the written or computer-entered descriptions of the gross findings recorded at the time of the necropsy. However, images may be captured at necropsy to help illustrate the written descriptions of the gross observations to the people reviewing the pathology report. These gross pathology images were taken of findings that had been already observed; they are not raw data because they are not the basis of the findings.

Illustrative images may be taken to show a particular color or pattern, lesion location, or lesion distribution. Sometimes images may include extraneous artifacts. For example, there may be a bright spot due to some reflected light, or a dark spot due to some clotted blood, or extraneous tissue, or some other debris on the part of the tissue surface within the image frame. These are all artifacts; but their true nature may not be readily discernible from the recorded image.

It is important to realize the inherent limitations of many gross pathology images. Even the very best possible images captured at necropsy can only provide fragmentary or incomplete information. During the necropsy, the tissue may be incised to follow and fully investigate a particular lesion. The complexity of the lesion regarding size, color, consistency, smell, and involvement of adjacent structures is best captured as text descriptions at the time of necropsy. For example, the size of a lesion in an image is dependent on the

single focal plane of the image, not the all of the various tissue levels aspects that were evaluated at necropsy. Thus, the gross written description lesion size may appear smaller than on the image; which can occur when a tubular structure is cut obliquely, but the particular gross photos was taken to illustrate the color variation in the lesion rather than lesion size. Since this complexity cannot be captured by an image, illustrative images cannot be readily used to supersede the gross written descriptions.

As previously discussed, for some types of studies, the protocol may require some images to be taken at the time of necropsy. The necropsy record is annotated to indicate that gross images were taken. It is common practice that at necropsy a set of gross images are taken of the same specimen at different focal planes or light exposures to ensure that some good quality images are taken. After necropsy, the illustrative images can be reviewed and the best images selected to illustrate the gross pathology findings. The selected images can then be archived as part of the documentation that images were taken at necropsy. The nonselected illustrative images can be discarded.

The selection of the best images is analogous to selecting which tissue specimens will be collected at necropsy and processed into specimens for microscopic evaluation, and which tissues will be discarded at necropsy. Illustrative images can be discarded because they are not raw data. However, whenever protocol-required illustrative images are captured, some of these illustrative images must be archived as documentation of completion of that protocol-required study activity.

In contrast to illustrative images, gross pathology images are raw data when they are used for data generation. For example, images may be captured at necropsy for subsequent morphometric analysis. The gross pathology images used for the morphometric analysis are raw data and must be authenticated at the time of data generation and archived and archived.

#### *Histopathologic/Cytologic/Ultrastructural Tissue Evaluation*

The pathologist may perform a histopathologic/cytologic evaluation of slide-based specimens using a light microscope, and/or an ultrastructural evaluation using an electron microscope. The use of an electron microscope to perform an ultrastructural evaluation of the tissues is a direct extension of the histopathologic/cytologic evaluation to higher levels of magnification and resolution beyond the capabilities of the light microscope, so the data/images are handled similarly.

Most of the time the study pathologist make their diagnoses while viewing tissues on the light or electron microscope, and the signed and dated report from the study pathologist is the raw data for this tissue evaluation. In addition, as previously discussed, when captured images (either photomicrographs or electron photomicrographs) are used by the study pathologist as the basis of their diagnoses and/or morphometric analysis, then those images are also raw data and must be authenticated and archived.

In contrast, illustrative images may also be captured for a variety of reasons, and generally they do not have to be archived. Illustrative images may be captured for use in multi-company collaborative nomenclature efforts, as previously discussed, or for use in pathology peer review, discussed in the next section; and these illustrative images do not have to

be archived. However, if illustrative images are included in the pathology report, then these images are archived with the report.

Also, illustrative images that are used as part of a regulatory response are also commonly archived for convenience to facilitate rapid retrieval for potential use in future responses. In addition, because electron microscopy (EM) specimens are not as durable as slide-based specimens (EM tissue specimens tend to desiccate, crack, and fall off the grid after about 1 year), it is a common practice, even if the pathologist makes the diagnoses while at the electron microscope, that some illustrative images are captured. These illustrative images are not raw data. However, commonly some of these images are archived as part of the documentation that an ultrastructural tissue evaluation was done on the study.

When reviewing microscopy images, an image may not provide a sufficient basis to reach the same diagnosis as was determined by the study pathologist who viewed the slide-based specimens. Most histopathologic/cytologic images capture only a small part of the specimens examined by the pathologist. In addition to the morphologic characteristics of the individual tissues/cells on a slide, the pathologist also considers the findings in other tissues from the animal, other sources of data (e.g., other clinical pathology data) and compares the changes observed in other treated animals and control animals from the study. Subsequent evaluation of additional slide-based specimens utilizing immunohistochemistry or special stains may also contribute to the final diagnosis. Therefore, even a review of the entire specimen on a slide may not be sufficient to confirm the pathologist's interpretation of microscopic findings, because a single slide does not represent all of the information evaluated by the pathologist in reaching their diagnosis.

Pathologists may create sets of illustrative images for a variety of reasons including: a series of test article-related findings for potential use in regulatory submissions; or as part of a reference set for teaching purposes; or a set for a multi-company nomenclature effort discussion; or a set of unusual or particularly interesting lesions for informal pathology peer review (discussed in the next section). Since these illustrative images are not raw data, there is no requirement to archive these images. However, selected properly labeled illustrative images may be archived from a study for convenience if the pathologist wants them to be readily retrievable in the future.

#### *Informal Pathology Peer Review*

Informal pathology peer review or histopathologic/cytology consultation before the pathology report is completed is a common practice in toxicologic pathology. This review most often occurs through sharing glass slide(s). However, this peer review could also be done using illustrative images. For example, the study pathologist could e-mail image to another pathologist(s) or use a tele-pathology system to facilitate discussion among pathologists at distant geographic locations. Also, a pathologist may send intentionally unlabeled electronic images to discuss a finding with colleagues at other companies working on a standardization of nomenclature and diagnostic criteria committee.

It is important to note that these informal discussions and any associated images are not pathology raw data. During an

informal pathology peer review, the opinions of any consulting pathologists are not binding on the study pathologist. 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), states that:

“... 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.”

Thus, records of informal consultations and any associated illustrative pathology images are all part of the study pathologist's interim notes (not raw data). Therefore, none of the notes or illustrative images needs to be archived.

#### *Formal Pathology Peer Review*

Similar to the informal pathology peer review, a formal review is done before the pathology report is completed. The associated records and illustrative images are all part of the study pathologist's interim notes; therefore, there is no need for them to be archived. A formal pathology review is performed on a study to provide assurance that the pathology diagnoses and data interpretation represent a consensus opinion of more than one pathologist. Any discrepancies in the diagnoses or data interpretation are resolved before the pathology report is signed. At the end of the formal pathology peer review, the reviewing pathologist prepares and signs a Peer Review Statement that describes the study material reviewed and confirms overall agreement with the interpretations and conclusions of the study pathologist. The signed and dated Peer Review Statement must be archived, and is commonly included in the final study report.

Virtual slides may be used to facilitate formal pathology peer review across distant geographic sites. If the study pathologist reviewed glass slides, but the peer-review pathologist reviewed virtual slides, then any discrepancies found during the peer review should be resolved using the glass

slides. The virtual slides are considered to be the pathologist's interim notes that can be discarded. In contrast, based on current technology and practices, if the study pathologist reviewed the virtual slides as the basis of their morphologic diagnoses, then the virtual slides used for data generation must be authenticated and archived along with the glass slides.

#### CONCLUSIONS

The Society of Toxicologic Pathology recommends that images used for data generation (e.g., the basis of a diagnosis or morphometric analysis) are raw data, and in contrast, that images not used for data generation are illustrative images that are not raw data. Based on current technologies and practices, any image used for data generation, becomes raw data at the time of data generation and at that time an image print or the electronic image record must be authenticated by specific annotation indicating when and who used that image for data generation, and also that image raw data must be archived.

When images are to be used for data generation, then procedures and controls similar to those for other data generation practices (e.g., written SOPs, testing/validation of equipment and training of personnel, etc.) must be in place to protect the integrity of the image raw data. Any GLP exceptions should be stated in the GLP Compliance Statement for the study. In general, illustrative images do not have to be archived, except when they are part of a final study report or when they are needed as documentation of protocol-required imaging. Finally, since illustrative images are not the basis of a diagnosis, they cannot be readily used to re-evaluate or supersede the pathologist's written diagnosis obtained from direct examination of the tissues at necropsy, slide-based specimens or ultrastructural specimens.

#### ACKNOWLEDGMENT

The recommendations in this paper are endorsed and supported by the American College of Veterinary Pathologists, and the British Society of Toxicological Pathologists.