EPL®

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Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Ref: Docket Nos. 03D-0060, 99D-1458, 00D1538, 00D-1543, 00D-1542, and 00D-1539

Dear Sir/Madame:

Experimental Pathology Laboratories, Inc. (EPL®) is a contract organization with over 30 years experience in regulatory toxicologic pathology. Many of our clients are from industries regulated by various agencies, including the Food and Drug Administration. We are submitting this letter to comment upon the draft "Guidance for Industry, Part 11 Electronic Records; Electronic Signatures – Scope and Application" issued in February 2003.

EPL recognizes the need for assurance that electronic records maintained under GLPs and other regulations are valid and secure and that records submitted to the agency under an electronic signature are true representations of the data. Therefore, we understand and agree that Part 11 regulations serve a valid purpose to that end. We commend the agency on devoting the significant resources and time required to develop and implement Part 11 as a framework for controlling the use of electronic records and electronic signatures. We believe the Agency's objective, i.e., "to permit the widest possible use of electronic technology, compatible with FDA's responsibility to protect the public health" is laudable. Overall, we acknowledge that the content of Part 11 was necessary and appropriate for ensuring the integrity of state of the art electronic record keeping.

We have had concerns with the interpretation of Part 11 requirements as stated by some FDA regulators in conversations, in public forums and in some of the Guidance's issued previously. Some of the interpretation provided seemed to unnecessarily burden the regulated industry and discourage, rather than encourage, the use of the latest technology in producing the records required by the Agency. We agree wholeheartedly with the Agency's conclusion that there is a need for review of the manner in which Part 11 requirements are to be applied. Therefore, we are extremely pleased to see that the Agency intends to revisit interpretation of Part 11 requirements as indicated in the February draft Guidance Document.

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Specifically, we believe that the Agency's intent to narrow the interpretation of the regulation is appropriate and that the incidental use of a computer to generate a record related to a regulated study does not, in and of itself, necessitate that record be subject to the requirements of Part 11. We completely agree that any electronic system used to generate, maintain, manipulate or store data from a regulated study should comply fully with the longstanding GLP requirements for system validation, audit trails, security, etc. We also concur that any use of electronic signatures should be subject to strict controls.

Naturally, our experience and expertise is focused in the generation of histopathology data for our clients. The accepted definition of histopathology raw data has been the glass slides and signed final pathology report. Since the issuance of Part 11, there has been much discussion about its applicability to electronic histopathology software systems. We believe that, under the predicate rule (21CFR Part 58), maintenance of security and validation of such a software system is necessary and appropriate. However, we also believe other requirements of Part 11 should not be applicable to histopathology systems. For example, we feel the Part 11-specified audit trail should be required for a direct entry pathology software system only after the pathologist has completed the tissue evaluation, finalized the diagnoses and locked the histopathology database. All prior iterations of the database should be considered interim notes rather than raw data and, therefore, not subject to the audit trail requirements of Part 11. In the case of more traditionally derived pathology data (i.e., dictated and compiled through conventional word processing), an audit trail should be required only for changes made after the pathologist has signed the final pathology report. All prior drafts of that report should be considered interim notes. These interpretation are consistent with the historical interpretations of the predicate rule.

Although our interest in Part 11 largely concerns its applicability to electronic pathology software systems, other aspects of our laboratory operation are subject to 21 CFR Part 58, and consequently may also be subject to Part 11 considerations. Many of these applications are not used wholly in electronic form and do not generate data or affect the evaluation and interpretation of the data. Therefore, they have a minimal impact on the overall compliance of any given study. For example, the Master Schedule that is required by the predicate rule may be generated and maintained by various software applications.
However, the Master Schedule is not raw data as defined by the predicate rule and is not required for the reconstruction or evaluation of the study. We agree that an electronic system used to generate the Master Schedule should comply with accepted standards for validation and security; however, the need for an audit trail appears unnecessary. The degree of reliance on the electronic copy of the Master Schedule within a facility should dictate its degree of compliance with Part 11 requirements. If printed copies of the schedule are used by the laboratory as the source of information, there is little to be gained from maintenance of an electronic audit trail. If the schedule is used exclusively in electronic form, then Part 11 requirements would seem more applicable.

Again, we agree wholeheartedly with the Agency's conclusion that there is a need for review of the interpretation of Part 11 as it applies to many routine electronically generated records during the conduct of studies subject to 21 CFR 58 requirements. We commend the Agency for initiating the review. We also thank you for your consideration of our comments on the recently issued draft Guidance document issued by CBER.

Sincerely,

Jerry F. Hardisty DVM

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President
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