

## EPA GLP Issues Associated with Electronic Data Collection.

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During the next 20 minutes, I will review fourteen basic GLP issues associated with electronic data collection using computerized systems.

Based on information obtained during American Cyanamid Company's Quality Assurance (ACCO QA) inspections conducted at multiple field research facilities over the past few years, it was observed that there was occurring a significant shift from direct recording of raw data on paper to first recording it via electronic data collectors, then printing it to paper. Also a few years ago, the EPA indicated that it would implement new regulations in the computer area, but fortunately moved cautiously to do so. Language regarding computers was incorporated in the proposed FIFRA/TSCA consolidated GLP rule issued on December 29, 1999 (40 CFR part 806).

This lag time allowed NAICC GLP researchers and their QA Units to work together with Cyanamid's study directors and QA Unit to test the new technologies, proactively identify potential compliance issues, and take corrective action in advance of the Agency.

By treating computers just as any other piece of equipment, Cyanamid's QAU identified potential compliance issues via recommendations in audit reports based on the existing GLPS. I want to thank all research and QAU staff at field facilities, and soil and RAC processing labs who have worked closely with me and other ACCO QA auditors during your critical phase and facility inspections.

To illustrate the fourteen basic GLP issues, I will use a computerized system for monitoring the temperature of sample freezers. Tim Vargas suggested I address electronic temperature data collectors, as other speakers at the meeting have discussed electronic notebooks. GLP basics are similar to all computerized systems, such as those shown below.

### EXAMPLES OF COMPUTERIZED SYSTEMS USED IN GLP DATA COLLECTION, GENERATION, or MEASUREMENT.

Computer plus:

- Temperature Monitor (e.g., test substance storage or sample freezers)
- Weather Station, single or multiple parameters (e.g., rainfall, air and soil temperatures)
- Balance
- Spreadsheet Program (e.g., to collect and process data)
- Random Number Program (e.g., to randomize plot layout)
- Electronic Notebook Program
- Email and Facsimile Programs (e.g., to distribute data)

First, I want to highlight four GLP compliance issues that were frequently observed.

1. Many facilities had excellent SOPs and Maintenance Logsheets for the temperature datalogger, but did not have any written procedures (other than the user manual) nor Maintenance Logsheets for the computer necessary to make the datalogger work. We had to change our thinking from focusing on the monitoring instrument alone, to the concept of a “computerized system”, the component parts of which may have been purchased separately. This observation is the foundation for the new proposed rule 806.63(d).
2. Training records were thorough for every piece of equipment where the field investigator trained a staff member, but there was no documentation of the self-training by the field investigator or of self-training by the staff.
3. The facility equipment inventory did not list the software used to operate the computerized system(s). If software is not adequately documented, it will be impossible to reconstruct what equipment was used to generate the data. Also, if a “bug” in a particular version/release of software is discovered in the future, you cannot assess the impact on your study if the version/release was not documented.
4. The facility SOP did not define what is considered to be the raw data, e.g., the first printout of the data table or graph versus the electronic medium on the personal computer. This omission is a potential GLP issue with what may be “raw data” in the proposed change in rule 40 CFR 806.3 (see Table II). The definition of raw data from computerized systems must be clearly defined in the facility SOPs.

Next, I need a little audience participation, so I can properly tailor the rest of my talk. Please raise your hand if your facility currently uses some type of computerized system for monitoring temperature. Put your hands down. Please raise your hand if you do not use a computerized system for monitoring temperature. Put your hands down. Thank you.  
[Comment on relative proportions observed.]

This has been an exciting meeting, and I know with the lateness of the day, you are probably becoming mentally saturated. So I have prepared a handout to minimize your need for notetaking. For the remainder of my presentation, I will discuss the thirteen basic GLP issues shown in Table I.

For those of you who raised your hands because you are using a computerized system, I would like you to mentally conduct a facility inspection. On your handout, note those areas which you could improve the quality of your compliance. For those of you who are not using such a system, or who plan to implement one this season, you can use the table as a checklist when developing your system.

Table I. EPA GLP ISSUES Associated with Electronic Data Collection (Computerized System; 40 CFR parts 160, 792, and proposed 806)

Example: Temperature datalogger (computer w/probe, measurement and initial data storage)  
+ Personal Computer (storing, processing and printing of raw and calculated data)

OPERATION/PROCEDURE/ACTIVITY	RECOMMENDED GLP DOCUMENTATION
1. Planning, equipment specification, QAU involvement	Specification document (user requirements)
2. Equipment purchase	<p>Equipment Inventory*</p> <p>Temperature Measurement and Datalogger</p> <ul style="list-style-type: none"> <li>• Hardware: Make, Model, Serial No.</li> <li>• Software, Version No.</li> </ul> <p>Personal Computer System</p> <ul style="list-style-type: none"> <li>• Hardware: Each Component Make, Model, Serial No. <ul style="list-style-type: none"> <li>✓ Computer CPU, monitor, keyboard</li> <li>✓ Printer</li> <li>✓ Network servers</li> </ul> </li> <li>• Software, Version No. <ul style="list-style-type: none"> <li>✓ Operating system (e.g., Windows 95)</li> <li>✓ Spreadsheet</li> <li>✓ Random number generator</li> <li>✓ Facsimile letter</li> <li>✓ E-mail</li> <li>✓ Virus detection</li> <li>✓ Y2K testing</li> </ul> </li> </ul> <p>* Separate document or as part of maintenance log</p>
3. Installation Testing (vendor or self)	<ul style="list-style-type: none"> <li>• Documentation</li> </ul>
4. Validation Processes. An ongoing process of testing to demonstrate that the computerized system reproducibly performs what it is designed to do.	<ul style="list-style-type: none"> <li>• 160.63(a), 806.63(d) proposed</li> <li>• Validation plan, testing, report</li> <li>• Validation by verification of raw data</li> </ul>
5. In-house Software development	<ul style="list-style-type: none"> <li>• Printouts of code, spreadsheet cell formulas</li> <li>• Changes to code</li> </ul>
6. Write SOP(s) covering procedures for use of both temperature datalogger <u>and</u> personal computer system, including all the following topics 7-14.	<ul style="list-style-type: none"> <li>• 160.63(b), 160.81(b)(10), 160.81(b)(11)</li> <li>• 160.130(e), Dated signature on raw data</li> <li>• 160/806.3, Define what is raw data</li> <li>• User Manuals for all system components</li> </ul>

OPERATION/PROCEDURE/ACTIVITY	RECOMMENDED GLP DOCUMENTATION
7. User Training 160/806.29(a)	<ul style="list-style-type: none"> <li>• 160.29(b)</li> <li>• In each user's training record, enter self-training <u>and</u> training by another person</li> </ul>
8a. Periodic Equipment Testing, etc. (hardware and software); Revalidation. E.g., calibration/verification of probe accuracy	<ul style="list-style-type: none"> <li>• 160.61</li> <li>• 160.63(a)</li> <li>• 806.63(d) proposed</li> <li>• Periodic testing data</li> </ul>
8b. Y2K Testing	<ul style="list-style-type: none"> <li>• Report of Y2K testing (separate or part of Maintenance Log) <ul style="list-style-type: none"> <li>✓ Computer software</li> <li>✓ Datalogger software</li> <li>✓ February 29, 2000</li> <li>✓ Manufacturer certificates</li> </ul> </li> </ul>
9. Operate System	<ul style="list-style-type: none"> <li>• Raw data [dated signature; 160.130(e)]</li> <li>• Calculated data</li> <li>• Use Log (optional)</li> </ul>
10. Equipment Maintenance procedures (routine and non-routine) for both temperature datalogger <u>and</u> personal computer system	<ul style="list-style-type: none"> <li>• 160.63(c)</li> <li>• Maintenance log sheet – datalogger</li> <li>• Maintenance log sheet – computer system</li> <li>• Change control <ul style="list-style-type: none"> <li>✓ Software upgrades, including viruses and Y2K</li> <li>✓ Hardware addition (e.g., second hard drive)</li> <li>✓ Component replacement or retirement</li> <li>✓ Computer clock changed from standard to daylight time, or vice versa</li> </ul> </li> </ul>
11. Computer Security measures (password, computer in locked area)	<ul style="list-style-type: none"> <li>• 806.63(d) proposed</li> <li>• Access (list of persons and access level; changes)</li> <li>• E-mail and facsimile (electronic names)</li> </ul>
12. Disaster Recovery Procedures (also described in validation plan)	<ul style="list-style-type: none"> <li>• 806.63(d) proposed</li> <li>• 160.81(a)(10)</li> <li>• Virus protection and upgrades</li> <li>• Periodic backup of files to second medium</li> <li>• Reinstall files from data backups</li> <li>• Backup temperature systems [manually document freezing temperature if computerized system fails (e.g., inverted water tube, maximum/minimum thermometer)]</li> </ul>
13. Periodic Archival of documents, file backups, obsolete equipment	<ul style="list-style-type: none"> <li>• 160.190, 160.195</li> <li>• 169.2(k)</li> </ul>
14. Periodic QAU audits/inspections	<ul style="list-style-type: none"> <li>• Facility and study-critical-phase audit/inspection reports, 160.35(a-d), 169.2(k)</li> </ul>

Table II. Computerized System Changes to FIFRA/TSCA rules proposed 12/29/99 as  
40 CFR part 806

Replaced text [ ] in original 40 CFR parts 160 and 792. Proposed change to text is bolded  
and underlined.

**§ 806.3 Definitions.**

["Raw Data"] **Raw data** may include photographs, microfilm or microfiche copies, computer printouts, [magnetic media, including] **any original data captured electronically or by some other medium**, dictated observations, and recorded data from automated instruments.

**§ 806.29 Personnel.**

(a) Each individual engaged in the conduct of or responsible for the supervision of a study shall have **the appropriate** education, training, and experience, or a combination thereof, to enable that individual to perform the assigned functions.

**§ 806.63 Maintenance and calibration of equipment.**

**(d) The integrity of data from computers, data processors, and automated laboratory procedures involved in the collection, generation, or measurement of data shall be ensured through appropriate validation processes, maintenance procedures, disaster recovery, and security measures.**