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Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Subject: **Docket Nos. 03D-0060, 99D-1458, 00D-1538, 00D-1543, 00D-1542 and 00D-1539 Draft Guidance for Industry on "Part 11, Electronic Records, Electronic Signatures – Scope and Application"**

4 April, 2003

Dear Sir/Madam:

Thank you for the opportunity to comment on the Draft Guidance for Industry on "Part 11, Electronic Records, Electronic Signatures – Scope and Application" published in the Federal Register on February 25, 2003. Below are Genzyme's comments for your consideration.

1. We request that FDA state unequivocally that Part 11 is still in effect at the start of the draft guidance, as we have noticed many differing opinions throughout the industry and its vendors.

2. Please define the term "fewer records" in §III A. It is our expectation that FDA means that process automation software such as ladder logic, distributed control systems code/scripts/objects, parameter tables, configurable chips, etc. are no longer considered e-records for the purposes of requiring audit trails and enhanced security. However, robust configuration management processes (paper and electronic) would still be applied. We are unclear as to whether the concept of "durable media" as a defining factor when an e-record is created is still applicable. This would mean that less-complex equipment (pH meters, osmometers, TOC meters, etc.) generating a signal output directly to an LED or other visual device that may reside on a durable media until overwritten, are also exempt, with the exception of robust configuration management/metrology/SOP control programs already in place.

3. In §III A, it would be helpful if the items listed in the parentheses were directly related to the rule elements they reflect.

4. We request further definition of "enforcement discretion" mentioned in §III A, and some characterization of the enforcement process. Does FDA consider enforcement to be part of the escalation process detailed in the dispute resolution proposal at http://www.fda.gov/cder/gmp/gmpdispute.htm?

5. In §III B 1, please clarify whether the term *"merely incidental"* includes security and controls that enable us to prove that we have content integrity. We also request that FDA list classes of

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instruments or types of technologies covered by "incidental" use.

6. §III B 2, Bullet Point 2 suggests that hybrid environments will always be taken into account under the business practice considerations. We note that official documentation via SOPs will not assure that e-records versus paper records (or vice versa) prevail. How will FDA distinguish whether records or the context in which records are used fall under performance of a regulated activity?

7. We are unclear as to what the Agency intends in §III B 2, Bullet Point 3. It would seem that submission requirements are covered under predicate rule.

8. We note, in §III B 2 Bullet Point 4, that electronic signatures are not equivalent to "initials and other general signings." Electronic signatures are legally binding equivalents of handwritten signatures. We believe that FDA should provide clear distinction between electronic signatures as opposed to electronic identity (that which is achieved by logging in to a computerized system).

9. The first paragraph in §III C 1 suggests that audit trails do not necessarily require validation when a computer system is validated. Please confirm.

10. §III C 1 paragraph 2 states " . . . it may be important to validate the systems to ensure the accuracy and reliability of part 11 records contained in the system" in the absence of a predicate rule requirement. Please explain the distinction between tools (applications that create predicate rule e-records) and systems (that contain predicate rule records). For example, the use of Microsoft Word to create an SOP (a tool with a resultant electronic record) versus SAP (an application that contains predicate rule electronic records for product traceability and release).

11. Paragraph 2, §III C 2 seems to indicate all systems and interfaces require risk assessments as part of a central system validation effort, regardless of predicate rule influences. This seems inconsistent to us. Does FDA intend to be able to inspect such systems under routine agency visits? Please consider the following example. If a Human Resources management system passes information to a predicate rule training system, is the Human Resources system required to apply audit trails and controls to meet Part 11? Should an audit trail be applied at the interface level?

12. §III C 3 implies that a retired system or a static system does not have to be remediated. If a system was in existence prior to August 1997, (i.e., a legacy system) and the applicable application has since been upgraded, will the Agency apply "enforcement discretion" if the system is not Part 11 compliant? We believe that a legacy definition should be technology/function-driven rather than date driven, as the date only constitutes part of the story for achieving compliance. Also in this section, please clarify the phrase "fit for intended use."

13. Please elucidate the Agency's expectations during an inspection in §III C 4, specifically, what is considered "reasonable and useful access" to records during an inspection? Will FDA expect to review paper or will inspectors need to perform electronic system review? The requirement for ability to search, sort or trend implies that there may be a need to supply the

application. There are other types of files that could be considered "technology neutral" such as CSV. We note that "technically feasible" can usually be accomplished at great cost. We would like to ensure that our efforts produce usable data and materials for your inspectors. Please provide specific examples of what kinds of e-copies the Agency expects to be processable versus static.

14. In III C 5, does FDA expect access to electronic copies of retained records? In addition, does the Agency require electronic copies of audit trails, and are these audit trails expected to meet predicate rule retention requirements for their associated records? Please clarify.

We believe that overall the draft guidance has been helpful in interpretation of previous issues, e.g., clarification in the use of "technology-neutral" copy formats, but has raised further questions as noted earlier. In particular, we appreciate the enhanced use of risk assessment when applying Part 11 to different systems. We also believe that the ability to retain electronic record information in ways other than electronic form to meet long term retention periods is useful. Genzyme appreciates the opportunity to comment on the Draft Guidance for Industry on "Part 11, Electronic Records, Electronic Signatures – Scope and Application." Please contact me at (617) 374-7275 or Juliette Shih at (617) 761-8929 should you have any questions regarding this letter.

Cordially,

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