

July 8, 2004

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

Re: Docket No. 2004N-0133
Electronic Record; Electronic Signatures; Public Meeting

Dear Sir or Madam:

Amgen Inc. (Amgen) submits the following comments on the agency's regulations on electronic records and electronic signatures, as set forth in 21 C.F.R. Part 11 ("Part 11").

Amgen supports FDA's efforts to re-examine Part 11 in an effort to clarify the scope of the rules, to prevent unnecessary controls and costs, and to encourage technological innovation while ensuring an adequate level of record security, authenticity, and integrity. Amgen's comments focus on (i) the scope of Part 11; (ii) conflicts between Part 11 and certain predicate rules; (iii) use of a risk-based approach in more areas of Part 11; and (iv) the effect of Part 11 on the use of new technologies.

I. FDA should limit the scope of Part 11 only to explicit recordkeeping requirements.

Amgen recommends that FDA formally revise the scope of Part 11 by codifying the narrow approach adopted in the agency's recent Guidance for Industry, *Part 11, Electronic Records; Electronic Signatures – Scope and Application*, 68 Fed. Reg. 52779 (Sept. 5, 2003). In particular, Amgen urges the FDA to limit Part 11's applicability to only those records that explicitly are stated as such in a predicate rule. Part 11 should not apply to records inferred or generated to comply with predicate rule activities (e.g., records kept to demonstrate compliance with GMP requirements).

Also, Part 11 should not apply to records that may technically be covered by a predicate rule but not required to be *retained* under the predicate rule.

Finally, Amgen recommends that FDA adopt consistent Part 11 requirements for those electronic records actually submitted to FDA and those electronic records maintained internally by a sponsor to satisfy predicate rule requirements.

II. FDA should resolve conflicts between Part 11 and certain predicate rules.

Amgen urges FDA to examine potential conflicts between Part 11 and predicates rules set forth in 21 C.F.R. Part 312. We believe that harmonization is necessary in order for a sponsor to be able to comply with requirements in both parts.

Section 312.62(b), for instance, requires an investigator to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to a patient who is participating in a clinical study. Case histories include case report forms and supporting data such as signed and dated informed consents and medical records. Medical records typically include additional documentation concerning the treatment of a patient, including the investigator's progress notes, nurses' notes, and the patient's hospital charts.

In organizing and maintaining these case histories, hospitals typically utilize electronic medical record systems that are designed to meet the primary needs of its staff (including the clinical investigators) and the expectations of the overseeing authority (such as the Joint Commission for the Accreditation of Healthcare Organizations and the Department of Health and Human Services' Office for Civil Rights, which oversees compliance with HIPAA requirements). Neither the FDA nor the sponsor, however, have jurisdiction or control over the validation and configuration management of these systems. Yet section 11.1(b) appears to assign responsibility for validation and configuration to the sponsor. In many instances, the sponsor therefore has to request the clinical site to revert to a paper-based system to achieve compliance with IND requirements. This reduces a sponsor's ability to incorporate more efficient, innovative processes in conducting clinical trials.

Furthermore, the ICH GCP (E6) guidelines that have been adopted by the FDA establish standards for data capture and change control that are not reflected in 21 C.F.R. Part 312. FDA should examine the feasibility of harmonizing Part 312 with Parts 58, 210, and 211 for definitions of record, change control, and validation of electronic systems.

Finally, Amgen recommends that FDA adopt consistent Part 11 requirements for those electronic records actually submitted to FDA and those electronic records maintained internally by a sponsor to satisfy predicate rule requirements.

III. FDA should expand its use of a risk-based approach to Part 11 requirements.

Amgen believes that a risk-based approach is appropriate for all areas of Part 11. Any risk-based approach that is formalized and based on a scientific approach, such as the "precautionary principal," would ensure that electronic records have the appropriate integrity and authenticity and electronic signatures are legally binding and authentic. Some types of records, for example, might not necessitate as rigorous an audit trail or validation.

Furthermore, FDA should refine its definition of "accurate and complete copy" in section 11.10 by using a risk-based approach. Under the current definition, it is unclear whether a sponsor must conserve only the meaning of the electronic data, or all aspects of the electronic data. FDA's regulations pertaining to Good Laboratory Practices ("GLP") 21 CFR § 58.3(k) allows sponsors to maintain a certified exact copy in lieu of the original, recognizing that it is not

always possible to maintain an “accurate and complete copy” when electronic copies are maintained in different format. Companies also might find the value of retaining certain records to decrease over time. We believe that the agency should allow a sponsor to maintain the meaning of particular electronic data in an electronic format that preserves the reliability of the data.

Finally, Amgen considers a risk-based approach to be appropriate for data integrity and confidentiality. Thus, we encourage FDA to consider eliminating the distinction between open systems and closed systems. Applying different rules to these systems is unnecessary if FDA applies a broader and uniform risk-based approach to the records maintained within those systems.

IV. FDA must ensure that Part 11 requirements do not inhibit the use of new technologies.

We believe that replacing requirements for specific technical controls in Part 11 with risk minimization requirements for specific potential threats to electronic records would ensure that innovation and technical advances could be employed to comply with Part 11.

V. Conclusion

Amgen appreciates the opportunity to submit these comments and looks forward to working with the agency on this important initiative to re-examine its Part 11 rules governing electronic records and electronic signatures.

Sincerely,



Stanley Cooper
Senior Director Quality



Keith Brown
Director Information Systems