

To: Division of Dockets Management (HFA-305)
From: Vien Hua, Quality, Regulatory and Compliance, Sanofi-Synthelabo
Date: 11 May 2004
Subject: Docket No. 2004N-0133: Comments for the FDA Public Meeting

I have submitted my comments (below) on the issue presented under **Docket No. 2004N-0133, Electronic Record; Electronic Signatures; Public Meeting** to be held on June 11, 2004 at the National Transportation Safety Board Boardroom and Conference Center in Washington, DC.

- Comment:** It was recommended within the context of the *Guidance for Industry: Part 11, Electronic Records; Electronic Signatures – Scope and Application* that the FDA encourages a documented risk assessment in evaluating Part 11 records for their record retention and availability. While there is general consensus that risk assessments are needed, especially for “implicit” records that are not clearly defined in the predicate regulations, there is no definition or minimum standards set by the FDA to formulate the understanding of risk and risk-based approaches. This factor is critical since formalizing risk assessments will ultimately increase the cost and resources required for compliance. Consistent with FDA’s initiatives on risk-based approaches (2002), different risk management models have been used (GAMP 4 risk model, Hazard & Operability Analysis, Threats and Controls, and the Failure Mode and Effects Analysis, etc.) in various forms and degrees in industry. It is also recognized that for a computer system validation, risk assessments are taken and executed in various phases of the computer system’s development life cycle, either documented or undocumented. A guidance from the FDA on the definition of risk and how formalized risk assessments may be used, such as to justify an approach, focus on critical functions, or to support successful computer systems development, may be helpful to determine how risk should be documented for electronic records.

Question: A definition of risk and risk assessment is truly needed to clarify the intent of the risk-based approach as it relates to regulated and non-regulated records. Factors that trigger risks should be defined as well as non-prescriptive recommendations to assess and mitigate those risks. Are there plans to define risk assessment/management and how will these plans be presented to the industry?

- Comment:** The Part 11 regulation addresses the technical control requirements needed for electronic records as compared to their paper counterparts. However, there are not many technical control requirements for electronic signatures as compared to their traditional, handwritten signatures. As an example, the documentation of most paper-based batch records require verification of intermediate procedures or testing steps by a reviewer’s signature/initials and dating. There is no distinction in the Part 11 regulation between an approval signature and a signature/initials for verification or review purposes only. The context and meaning of the signature is different for both instances and this should be addressed for electronic signatures. As another example, there are no technical controls in Part 11 to address electronic records that are signed with handwritten signatures that could be applied electronically to the record (such as what the United Parcel Service uses on their remote computers to confirm delivery of a package) or it could be applied to a paper printout. Since the master record is in electronic format, signing a printout of the record does not exempt the electronic record from Part 11, as the case for “hybrid systems”.

Question: Are there any plans to consider and add additional technical requirements for electronic signatures to Part 11 that distinguishes the differences or meaning of electronic signature to their traditional, handwritten counterparts? How will handwritten signatures that could be applied to electronic record be handled?

- Comment:** The definition of Part 11 applies if the regulated data is transferred to durable media. For certain automated, manufacturing systems such as autoclaves, the electronic record of the sterilization run is automatically stored to durable media where the data cannot be altered. By procedural controls, the operator prints out the run information to a local printer. However, the system automatically re-writes over the existing data during a new run and the old data is replaced by the new data into durable media. By definition, the

autoclave is required to be Part 11 compliant, which means that an audit trail should be maintained. However, there are no predicate requirements that require audit trail capability for sterilization runs.

Question: Since a printout of the run is generated per procedural controls, the automatic re-write of data is considered low risk. How will audit trail functionality be addressed for systems like the autoclave whereby the nature of the functionality does not allow for system intervention? Due to the system's criticality, predicate rule requirements, and functionality, the application of audit trail may be considered on a case-by-case basis. If audit trail will become a necessary requirement in Part 11, it would be prudent to revisit the predicate regulation to ensure that specific audit trail requirements are associated with a regulated record. To anticipate for the change in the rulemaking of Part 11, will audit trail be added as a requirement of the regulated record in the predicate regulations as well?