

***Notice of Participation  
and Comments  
Docket No. 2006N-0464***



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**Docket No. 2006N-0464**

**Food and Drug  
Administration**

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# Notice of Participation

SAS respectfully requests the opportunity to present at the Food and Drug Administration's December 18, 2006 public hearing regarding:

- Electronic Submission of Regulatory Information, and Creating an Electronic Platform for Enhanced Information Management; [Docket No. 2006N-0464]

SAS supports and encourages FDA's evolution from a paper-based to an all-electronic submissions environment. We are prepared to offer solutions, services and guidance to assist FDA in reaching this attainable goal.

SAS has worked with FDA for 30 years, provide numerous solutions including those that facilitate the submission and review process. Concurrently, SAS has been supporting the pharmaceutical industry in their endeavors to develop safe and effective therapies. In recent years, our technology has evolved with the industry's mandate to adopt new clinical standards and to support electronic submissions to the FDA.

Today, SAS provides a secure hosting environment for a number of pharmaceutical companies. In addition, we have already negotiated a comprehensive federal Department of Health and Human Services procurement vehicle to facilitate the purchase of submission, reporting, analytical and reviewing software solutions.

SAS' preliminary recommendations for transitioning to an all electronic submissions environment are provided in the subsequent section.

We welcome the opportunity to further elaborate on our comments at the public hearing. If granted this opportunity, our desired time for presenting is 30 minutes.

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# Comments on Section IV Topics

SAS has chosen to respond to a number of areas in Section IV of this docket, based on the experience we have gained from FDA and our pharmaceutical, medical device, and CRO clients' implementation of SAS software and solutions. This software includes many tools for:

- Managing and integrating large amounts of data.
- Transforming clinical data to current CDISC standards
- Analyzing clinical trial data to determine the safety and efficacy of a therapy.
- Implementing a regulatory compliant electronic platform that serves as an environment for data management, analysis and reporting of study data.

Following are SAS' preliminary high-level comments in response to selected discussion topics in the docket. For ease of reference, we have retained the numbering scheme of that document.

## *IV. Issues for Discussion*

### **A. Electronic Submissions**

#### 4. Implementation

- *Should we consider an incremental phase-in implementation strategy for an all-electronic submission environment? Is so, what should the strategy include? What is the order of priorities for phasing in implementation?*

SAS Response: Rather than considering the submission as a transmission of information that occurs at the end of a process, SAS recommends considering it a collaboration (i.e., "continuous marketing application," "rolling review").

From this perspective, we believe that the implementation strategy should involve establishing a common workspace with common tools

that provides for a true partnership among sponsors, the industry and the agency. We further recommend that this common workspace be based on electronic platform that would support the e-CTD lifecycle management from the initial IND through the pre-approval marketing application.

We envision that this common workspace will allow companies to work in a private workspace before publishing to the sponsor/review committee workspace. The toolset associated with this workspace could come out of a concept similar to the Open Toolbox.

➤ *What steps can we take to minimize the cost or other burdens of transitioning to an all-electronic submission environment?*

SAS Response: FDA can minimize the cost and burdens of transitioning to all-electronic submissions by implementing the solution as a hosted, shared system that all parties (sponsor, CRO, FDA) would be able to access in a secure and controlled manner. All authorized users that with Internet access, regardless of location, will be able to access the system.

This type of implementation will minimize software development costs, implementation resources, installation, validation and training. Moreover, a hosted model will free FDA's IT organization from having to install, upgrade, maintain and support the new systems.

In addition, a hosted solution would feature 24/7/365 technical support and provide a guaranteed uptime service-level warranty.

➤ *What additional standards or revisions to current electronic standards would be helpful to make electronic submissions work?*

SAS Response: Simplification of the standards for submission would help both vendors and sponsors. CDISC is an open standard and available to all organizations, but implementation of those standards and software tools to implement the standards are not readily available or open. The electronic platform must accommodate and support the implementation of CDISC standards, particularly SDTM, but other CDISC models that would also be used during the submission development process.

➤ ***Are the tools and formats currently available for FDA electronic submissions adequate? If not, why? What is needed?***

SAS Response: The industry uses a diverse set of tools to build and maintain e-submissions. The adequacy of the various tools is not well established in many circumstances. SAS Transport format is an open source format readily available. Other open source formats are not common or available. An open set of tools with interfaces to common tools used in the submission process is needed.

The FDA has CRADA-based tools available for reviewing submission, but such tools are of limited value in preparing the submission. These tools are typically used with a mind to addressing FDA questions when they arise, but are not intrinsically part of the submission process. As such, they place additional burden on the sponsor, who has to prepare the submission using one set of tools, and be ready to perform an internal review of the submission using another. Additional tools, based on the submission development process, would have value to industry in establishing a prescribed method for building the submission.

Some technology companies (including SAS) have developed tools to create SDTM formatted XML, but many in the industry are not aware of their availability. Sponsors have also not applied the tools, because SDTM in XML is not yet required and the agency may not be ready for that submission. A tool to support CRTDDS (define.xml) could be developed collaboratively with the industry as the Study Data Specifications of the e-CTD final Guidance go live in 2007-2008.

➤ ***Are there other submission mechanisms more suitable and beneficial than what is currently available (e.g., the electronic submission gateway)?***

SAS Response: To reiterate SAS' earlier response, we believe the processes of submission, review and response should be re-cast as an ongoing collaborative process, based on a continuous marketing application or rolling review. In this case, a single transmission of content to FDA would not occur; instead, a common workspace would be used for collaboration of the submission and review.

- *Are there factors, such as data formats or tools, for harmonization with other government entities, the private sector, or foreign regulatory authorities that could reduce costs or increase the benefits of electronic submissions?*

SAS Response: There is certainly potential to harmonize business processes across multiple domains. However, for now, the focus should be on the submission/collaboration process between the pharmaceutical industry and FDA.

- *Would issuing guidance be useful in helping with the transition? If so, what topics would you like addressed?*

SAS Response: An FDA guidance would be useful in helping with the transition. As an example, providing the guidance on the use of CDISC SDTM provided direction that helped the industry with adoption of the standard.

## **B. Third Party Entities**

- *What are your general viewpoints on a third party entity or entities providing services related to such an electronic platform?*

SAS Response: From SAS' experience providing a hosted, regulatory compliant electronic platform for global pharmaceutical companies, it is important for the third party entity to maintain neutrality in the services they offer.

Capabilities should be limited to product (electronic platform), hosting, and technical support. The ability to provide "value-added" services to the sponsor or agency should be possible only in an openly competitive environment (other parties should also be able to provide the same type of services). Under no circumstances should the third-party have privilege to read or extract the submission content.

➤ *What are your views on the establishment of a public-private partnership to initiate formation of an electronic platform?*

SAS Response: A public-private partnership is probably the best compromise to meet the federal mandates for FDA regulated products and simultaneously obtain commercial innovation and enterprise to provide this electronic platform.

➤ *How do you envision the business process modeling and nature of the third party entity or entities?*

SAS Response: The third party entity/entities must represent themselves as a trusted third party between the sponsors and FDA. The entity must have a strong and viable track record in the industry for providing the software platform, tools and services needed. The business process modeling would need to be facilitated by the entity, but not necessarily owned by that entity. Those processes would need to be agreed upon by both the industry and FDA, with the third party agreeing to support those processes. The entity would need to be able to demonstrate the capability and willingness to sustain the platform and serve the needs of all parties using the platform.

➤ *What are the necessary attributes and characteristics of the third party entity or entities?*

SAS Response: see first bullet and bullet immediately above.

➤ *What services could the third party entity or entities provide?*

SAS Response: The third party entity should primarily provide services related to the implementation of the infrastructure needed to connect a sponsor and/or related parties, such as CROs, as well as the agency, to the electronic platform. Technical support and advisement on the use of the platform would also be appropriate. Additional services, such as back-up and recovery capabilities, change control/version control and disaster planning should also be available. Training on the use of the system could be made available, but other parties should also be able to provide services on the use and implementation of the electronic platform.

- *What collaborative efforts by FDA with a third party entity would be beneficial to establish services?*

SAS response: It has been our experience that it will be essential that a collaborative framework be established between the FDA and the trusted third party, including (but not limited to) establishing security mechanisms, user personas, change management procedures, and policies for governance of the electronic submissions platform.

## *Additional Comments*

### **Recommended Attributes of a Third Party-Managed Platform**

To fully meet the needs of FDA and its stakeholders, a third party-managed electronic platform must address a number of key technical and functional requirements. SAS recommends that such a platform must:

- Provide a 21 CFR Part 11 regulatory compliant, validated environment for storing and managing any regulatory submission artifact, whether full eCTD or partial update.
- Provide physical (data center) and user security.
- Scale sufficiently to handle large numbers of sponsors, users, and FDA reviewers.
- Meet expectations regarding the performance of the system, so that the platform does not become a bottleneck in the submission process.
- Feature a registry and repository master data management system that allows the agency to store and manage any artifacts of a submission, including data, programs, reports, documents.
- Be a metadata-driven solution designed (and open) to work with other industry applications relevant to the preparation and execution of a regulatory submission.
- Include built-in applications for loading, exploring, analyzing, and reporting data.

- Provide a Web-based portal for intra-FDA as well as external team collaboration with sponsors and their agents (e.g., CROs).
- Be built as an extensible platform that can integrate with FDA's existing tools, applications, and systems, as well as third party tools.
- Be supported in an ASP-hosted environment in a secure data center that has passed all regulatory audits.
- Include flexible workflow capabilities that automate the process of eCTD movement, data integration, user notification, etc.
- Provide validated integrations with common industry clinical review tools.
- Support the end-to-end interface of HL7/CDISC process flow to allow the transparency of the data collection and submission workflow.
- Upload data elements as required to a common repository for cross-study review of safety or efficacy.

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