

Industry Coalition on 21 CFR Part 11

Recommendations for Achieving Compliance with the Electronic Records and Electronic Signatures Regulation

29 August, 2000

Industry Coalition on 21 CFR Part 11

Recommendations for Achieving Compliance with the e-Records and e-Signatures Regulation

Background

In response to last February's meeting between FDA and PhRMA, PhRMA invited a number of other trade associations to form an Industry Coalition on 21 CFR Part 11 (hereafter referred to as the Coalition). The Coalition's objectives are to serve as a forum to represent a broad industry perspective, to discuss industry concerns and to collaborate with FDA to facilitate a workable implementation of the 21 CFR Part 11 rule (hereafter referred to as the Regulation). The Coalition will also seek appropriate opportunities to work with professional organizations to leverage their work on implementing the Regulation.

The Coalition currently comprises the following trade associations covering the major regulated industries:

1. Advanced Medical Technology Association (AdvaMed)
2. Consumer Healthcare Products Association (CHPA) – [Chair: William W. Bradley]
3. Cosmetic, Toiletry and Fragrance Association, (CTFA)
4. Council for Responsible Nutrition (CRN)
5. Generic Pharmaceutical Association (GPhA)
6. National Food Processors Association (NFPA)
7. Pharmaceutical Research Manufactures of America (PhRMA)

Value of the Regulation

The Coalition recognizes the value delivered by the Regulation in providing criteria and key principles for accepting e-Records and e-Signatures as a viable alternative to paper and to hand signatures. The Regulation has already benefited the industry and the FDA by enabling the *electronic* submission – without paper copies, and review of various components of marketing applications, e.g., adverse drug reactions (ADRs), case report forms (CRFs), etc. Eventually, the Regulation will facilitate both industry's and FDA's use of more efficient and effective business processes using e-Records and e-Signatures to replace many cumbersome paper-based processes. Thus, a pragmatic approach to interpreting and implementing the Regulation would aid in avoiding mistakes and fraud, preserving and protecting electronic GxP records, and maintaining both product quality and data integrity. It could, and most likely would, lead to harmonization of e-Records and e-Signatures within and across agencies and the regulated industries. It would also help to provide clear requirements specifications to key commercial software suppliers.

Coalition Position

The Coalition supports the general principles embodied in the Regulation and believes that it helps to address the paradigm shift involved in the move from paper records to electronic records. However, the extensive experience that has now been gained from attempting to implement it within the regulated industries has highlighted a number of difficulties giving rise to significant costs and risks that may outweigh the benefits. The scope of the Regulation is very broad having expanded from the original drug batch records to cover all GxP information collected with an electronic component. To

keep compliance efforts, burden and cost within reasonable bounds it is necessary to remember that one does not have to do something simply because one is capable of it.

Coalition member companies are concerned and are struggling to comply with the Regulation. The lack of both clear FDA guidance to industry and field inspectors (compliance policy guides), as well as the diversity in the interpretation of the Regulation, has led to widespread difficulties and confusion. Companies are investing million of dollars in “good faith efforts” to comply with the Regulation. Unfortunately, there is only limited assurance that the results of their investments and efforts will satisfy the Regulation. In some cases, the uncertainty in interpretation of Part 11 is leading to the deferral of IT investments that would otherwise have been available to enhance product quality.

A workable approach towards compliance needs to be developed. The Coalition believes that a dialogue with FDA is the best avenue to achieve this. We propose to work with the FDA to achieve a successful implementation of the Regulation, providing sufficient time for compliance and a realistic interpretation of the requirements that ensures high product quality while taking account of the available technology and overall level of cost to the industry.

Recommendations

The following recommendations are offered as constructive solutions to achieve implementation of the Regulation and are based on a realistic assessment of the time and expense required together with the risk associated with modifying/replacing current systems and their related business processes:

1. Electronic Records and Signatures

As a starting point, the requirements for electronically signed electronic records should be the same as for current paper records. This would also form the basis for the required audit trail recording all changes to an electronic record once it has been electronically signed. As with paper records, the point at which an electronic signature was applied would define the creation of an electronic record subject to the requirements of an audit trail. This would simplify the implementation of the Regulation, reducing the volume of data to be archived and simplifying the audit trail requirements so that they could be handled using normal database techniques.

The use of computer printouts as “raw data” has long been an industry standard and acceptable to the FDA. Applying handwritten signatures and dates to these printouts has been a widely accepted practice that should still be allowed. Application of the Regulation should not eliminate these accepted practices. A PDF image (an already accepted electronic standard by ICH, FDA and the regulated industries) provides the equivalent of “electronic paper” and should be acceptable as an electronic form of “raw data”.

2. Implementation Timing

The current validated systems are adequate to produce safe and quality products. Hence, compliance with the Regulation should be required only as they need to be replaced or upgraded as part of their normal life cycle. Replacing or upgrading them to achieve compliance with the Regulation outside their normal life cycle results in major cost projected to be billions of dollars for the regulated industries. This major cost would ultimately be borne by the consumers who purchase the products of the affected industries.

Attempting to replace/upgrade such a large number of applications, many of which are highly integrated, without adequate time, also introduces an unnecessary level of risk into the system and to consumers. This is clearly inconsistent with the intent of the Regulation and runs counter to FDA mission to protect the public health.

Therefore, we propose that existing applications, which may be a mix of electronic and paper-based records/signatures, and which are compliant with GxPs, should only incorporate those aspects necessary to comply with the Regulation as part of their normal replacement/upgrade cycle. For the majority of applications and related business processes, this would typically occur over 5-7 year life cycle. Some major applications, however, may have a longer life cycle. In addition, specialty computers, such as programmable logic controllers, which lack the ability to generate audit trails and/or extract data to external files, should be treated similarly.

Thus, each company would identify every application affected by the Regulation and develop a realistic replacement/upgrade plan in-line with its normal life cycle. This plan would be updated periodically to reflect incremental improvements. This list of all affected applications and the progress made against these plans would be made available for FDA inspections, if requested, during their inspections.

3. Risk/Benefits Driven Approach

Different control mechanisms should be applied to e-Records with respect to their potential impact on public health. Where the Regulation is applicable, a hierarchical approach to implementation of the Regulation to applications, data and reports should be applied. This approach is similar to the FDA's handling of post-approval manufacturing changes for pharmaceuticals (SUPAC). Since everything cannot be done at once, we propose developing a benefit-driven approach acceptable to both the FDA and the regulated industries.

Thus, each affected application in the list discussed above would be identified and ranked with expected benefits. Similar ranking would be established for data (by type) and documents (by type, e.g., SOPs, reports, etc) with each application.

4. Commercially Available Software

Regulated industries rely heavily on the use of mature commercial products from established market leaders and, typically, take a conservative position regarding the adoption of new technologies. Therefore, companies are extremely dependent on vendor software and their compliance with the Regulation. Few, if any, companies are prepared to revert to major custom in-house software development.

Vendors typically take 18-36 months to provide major new software releases, thus limiting the industry's ability to respond rapidly. New and unproven technologies often take significant time to mature and become incorporated in major software packages. In the early stages there may be problems with the reliability and scalability of these products. For example, it is currently hard to identify more than one off-the-shelf product for document management, submission publishing or adverse drug event reporting, and none of these is currently compliant.

Once FDA guidance documents and field inspection standards become available, the number of software packages from major vendors that facilitate compliance can be expected to increase. Software vendors, however, must be given adequate time to respond with sufficiently mature products with the new required functionality and technologies, such as e-Signature and Public Key Infrastructure. The industry will then need time to implement these new systems and modify related business processes including validation, user training, documentation etc, to meet business needs, GxPs and the Regulation.

Thus, the list of software applications above would include realistic time frames to adopt new off-the-shelf system that require minimum customizing. The Coalition will cooperate with vendors to facilitate rapid development of the required products.

5. Long-term Archiving

The impact of the rapid obsolescence of technology should be considered in defining long-term archiving requirements for electronic data and documents. Advances in electronic storage media and IT standards will inherently render current technology obsolete and eventually non-maintainable. Additionally, new generations of database technology generally appears in about 10-year cycles. Long-term electronic archiving is a complex task and the agency and the regulated industries should work together to develop a viable approach.

6. Economic Impact Analysis

An Economic Impact Analysis should be conducted to assess the additional regulatory burden on the regulated industries and to guide an appropriate implementation of the Regulation. This analysis should include the economic advantages gained and additional health benefit to the public resulting from the regulated industry's implementation of the Regulation. It is important to recognize that although some elements of the Regulation are described as being voluntary, they are in practical terms required. In addition, the regulatory requirements must be consistent with other government initiatives, such as the Paperless Environment 2002, Paperwork Reduction Act, the Mutual Recognition Agreement (MRA), and any new or pending legislation.

Guidance

These six points should be reflected in clear guidance(s) from FDA to the regulated industries and in compliance policy guides. The guidance should include a description of the interpretation and implementation of the Regulation and expectations of a "good faith compliance effort." The regulated industries should be given ample opportunity to provide early input to the development of the guidance(s).

Summary

The Coalition will,

- Lead the regulated industry and cooperate with FDA in realizing the benefits of the Regulation through a common interpretation.
- Provide qualitative and quantitative data for use in a constructive setting to work with and through the FDA and other regulatory agencies within (and outside) the United States.
- Provide a means for coalition members and others to benchmark current best practices, both procedural and technical.

The regulated industry and the regulatory agencies have a common goal in protecting public health and promoting best practices. Adopting a collaborative approach in this area of common interest should help to ensure that the regulated industries understand the FDA's requirements better and that regulations are based on current "Best Practices" within the industry. In addition, there is need to consider the level of costs and risk associated with changes to company systems/processes required to comply with the Regulation. By working together in this area, FDA and the regulated industries can ensure that the public has access to consistently high quality products at reasonable cost.

8/30/00