

*Johnson & Johnson*  
PHARMACEUTICAL RESEARCH  
& DEVELOPMENT, L.L.C.

920 Route 207, P.O. Box 300, Raritan, NJ 08869

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Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane  
Room 1060  
Rockville, MD 20852

**Re: Docket No. 00D-1539, Draft Guidance for Industry; 21 CFR Part 11; Electronic Records;  
Electronic Signatures, Maintenance of Electronic Records**

We welcome the opportunity to provide our comments on the *Draft Guidance for Industry 21 CFR Part 11; Electronic Records; Electronic Signatures, Maintenance of Electronic Records*. Our organizations are global biotechnology and pharmaceutical companies with years of experience managing paper records and electronic systems in a GxP environment.

These comments represent the consensus opinion of the following companies:  
Johnson & Johnson Pharmaceutical Research & Development, LLC  
Centocor, Inc.

This document presents general comments followed by comments on specific sections of the guidance.

Electronic records are not just in document form

Many of the topics and examples in the guidance are relevant to documents, but do not adequately address other forms of electronic records. Electronic records may also be maintained as, for example, relational data bases, files of instrument data output, images and new proprietary file formats supporting emerging scientific techniques and information technologies.

We recommend that all topics in the guidance are either:

1. relevant to all forms of electronic records (i.e.: does this guidance make sense for relational data bases?)
2. or specify a specific form (i.e.: an example might make sense only when applied to a document)

The unique challenge of records maintenance

Many of the requirements of Part 11 are reasonable and increasingly feasible in new systems today. However, the technologies and standards needed to maintain records electronically over long periods are not yet available and could prove to be extremely costly. Couple that with the exponential growth in data generated, and the risk of compliance with records maintenance requirements could prove to be extremely costly without any significant benefit to public health.

We recommend that the Agency clearly allow a risk-based approach to records maintenance in this guidance.

This guidance should be structured to ensure that Part 11 is not a reason for failure to adopt valuable technologies such as Process Analytical Technology (PAT). For example, it should be possible to define and validate that a clearly specified reduced data set is all that need be retained for the full retention period.

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In this approach, some raw data would be retained to support the validation of the data reduction method, but long-term retention of all raw data would not be required.

Clear definitions are needed

Agency and Information Technology professionals often use the same words in significantly different ways. The use of terms in any guidance when not clearly defined creates confusion.

We suggest presenting definitions with each guidance and then moving them to a glossary. Some terms that need definition include:

- Reprocess
- Reconstruct (as in Part 58)
- Archive
- Backup
- Metadata
- Authenticity
- Trustworthiness

Definitions should include lists (“not limited to”). Theoretical definitions like “Metadata is data about data” are not useful because some data about data (for example, how frequently data is accessed on a hard drive) would not be needed to meet the requirements of the regulation.

Comments on specific sections of the guidance follow:

Section 2. Scope

The scope of the document should be clarified to emphasize the maintenance of electronic records only. It should clearly restate or refer to comment 71 of the preamble to Part 11, which says that there is no requirement to maintain retired or obsolete software and hardware.

Section 4.2

“... electronic records ... must be retained for as long as the predicate rule requires.”

Predicate rules were mostly written for a paper world where records were usually documents. Now, many records are composed of multiple data elements in multiple tables in relational databases and never exist as a single “object”. And, in many cases, records as defined in predicate rules exist across several different computer systems, with parts of the record perhaps still remaining on paper.

We recommend that the guidance clearly acknowledge that electronic records can be composed of multiple data elements, and that when electronic records are migrated to new systems or removed from active use the original look and feel and some data precision may be lost.

Further, we recommend that the guidance explicitly allow that industry will achieve compliance only over time as marketplace solutions and industry standard data formats evolve to meet the requirements of the regulation.

Ideally, predicate rules should be reviewed and clarified:

- to reduce ambiguities (Part 58 should redefine “automated data collection system” to clearly include or exclude “manual entry of data into a computer” )
- to use appropriate computing terms and concepts ( what is the electronic equivalent of “initials”?...something that is clearly stated in several rules)

Section 5.5 “The Ability to Process an Electronic Record’s Information Throughout Its ...Retention Period...” Maintaining the ability to process information for the full retention period is potentially the most controversial and troubling issue we face in implementing Part 11. Even with this guidance, it is not clear to us what the Agency expects us to do. Some have read this guidance as defining a new requirement to be able to *reproduce* (literally) any record. On the other hand, this section could be saying only that data must be retained as data and not turned into a .pdf file, which is a picture of data, and does not easily lend itself for use in further calculations.

If the intention is to create a new requirement that industry provide the capability to perform calculations on archived or migrated data that produce results 100% identical to the calculated results in the original computer system, this will result in significant costs – far in excess of the benefit to the public health.

Computers differ in the way they handle basic math functions. This can lead to differences in rounding when the exact same calculations are run on two different computers. In some situations, this difference might be significant and in others, the difference might be in digits that are insignificant. We suggest that one solution is to document the minimum detail or precision required to meet the intended purpose of the record. This would allow a subsequent difference in a record to be seen as insignificant.

Acceptable alternatives are addressed in the predicate rules. For example in the GMPs section 211.180 (d) and the GLPs section 58.195 (g), the rule states “Records required by this part may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records.” This clearly shows the intent to retain the information and does not require reprocessing. Requirements for reprocessing should be limited to those stated in a predicate rule and not introduced through Part 11 guidance(s).

Another option is to use the concept of “reconstruction” (already used in Part 58) rather than “reprocessing” where, as needed and given some time, the processing of a record could be recreated using current programming and tools – recognizing that the look and feel will differ.

Section 6.1.2.3 “Where a migration, in effect, creates a new electronic record (by transforming the old electronic record) then, per section 11.10(e), the audit trail for the migrated electronic record would have to cover this creation. By adding this new creation step to the migrated audit trail carried over from the old electronic record you will help ensure a continuity of electronic record integrity.”

In systems using relational databases, moving data to a new system usually involves changes to:

1. the data mapping (where there is no 1 to 1 correspondence between data fields in the old and new system) and
2. the coding of data (where a “2” used to mean “hypertension” but now is coded as “7”)

The first problem cannot be managed in any audit trail scheme used today. The second problem requires clear guidance. Finally, almost no commercial software can accept the importation of audit trail data from a separate system.

Guidance should clearly allow the retention of original audit trail data in separate electronic files or tables where it is not possible to move the original audit trail data into the new system.

Where there is no loss of meaning or content, guidance should clearly allow the restating of coded data (changing a “2” to a “7” or “hypertension”) by means of validated scripts or macros and associated documentation of the coding changes, as an alternative to capturing the change in the audit trail. Guidance should also allow the destruction of electronic codelist metadata from retired systems when adequately documented in the validation of the migration and/or the retirement.

Section 6.2.1.5 “Unavoidable Differences And Losses...”

We are pleased that the Agency recognizes the fact that such events are “unavoidable”. Unfortunately, the realities that create differences and losses apply to all data in a system – not just those that are not mentioned in the predicate rules.

Instead of disallowing “differences and losses” in records required by predicate rule, the guidance should allow industry to define the requirements of data and records in a system and then allow any differences or losses that are not significant to the meaning of the data.

“...provided that differences are appropriately accounted for, and explained in either the migrated record or readily available *electronic* documentation.” (emphasis added)

This suggests that all explanations of losses or modifications must be electronic, and perhaps a part of the active computer system. The majority of commercially available software cannot support this requirement. Requiring all documentation to be part of the system or electronic is unnecessary to preserve the integrity of the data and would represent a burden on industry with no value in preserving the public health.

We recommend that the guidance not suggest that documentation that describes the creation, modification, migration or retirement of an electronic system be electronic just because the records themselves are electronic.

“...a trusted third party...”

We are pleased that the Agency is presenting detailed examples to help clarify their concerns. Of course, this creates new questions.

We recommend that the guidance clarify that “...a trusted third party from outside of the organization” does not have to be a separate legal entity but can be an independent group within the same firm.

“Color code changes; ..”

We are pleased that the Agency is presenting complex examples to help clarify their concerns. In this example, we find the explanation somewhat confusing, for example:

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“.. text (that referred to the colors) in the migrated electronic record should not be altered because doing so would change the record content and authenticity.”

This requirement would lead to potentially serious errors in human viewing of the record. We recommend that this section be rewritten for clarity. In our view, it is sufficient to document the mapping for the conversion and then use the new colors?

We believe these comments can be useful to the Agency in developing the final guidance.

Sincerely,

A handwritten signature in black ink that reads "Michael Weis". The signature is written in a cursive, flowing style.

Michael Weis  
Director  
Information Management Quality & Compliance  
Global Information Solutions  
Johnson & Johnson Pharmaceutical Research & Development