

David W Blois, Ph D  
Senior Vice President  
Global Regulatory Policy

Merck & Co., Inc.  
West Point PA 19486  
E Mail david\_blois@merck.com  
Tel 484 344 2304  
215 652 5000  
Fax 484 344 2335

December 4, 2002



Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, rm. 60  
Rockville, MD 20852

**RE: [Docket No. 00D-1539] *Draft Guidance for Industry, Part 11 of Title 21 of the Code of Federal Regulations (CFR): Electronic Records; Electronic Signatures, Maintenance of Electronic Records***

Merck & Co., Inc. is a leading worldwide human health product company. Through a combination of the best science and state-of-the-art medicine, Merck's research and development (R & D) pipeline has produced many of the important pharmaceutical and biological products on the market today.

Merck Research Laboratories (MRL), Merck's research division, is one of the leading US biomedical research organizations. MRL tests many potential drug candidates at one time through comprehensive, state-of-the-art R & D programs. There are three main stages to Merck's R & D process: basic research or discovery, followed by developmental studies in animals and manufacturing quality assurance testing, and, finally, human clinical research. The medicines that Merck ultimately presents to worldwide health authorities for marketing approval are those that have met the highest technical standards available and those that are able to withstand the most critical regulatory review.

In the course of bringing our product candidates through developmental testing and clinical trials, Merck scientists regularly create, archive, retrieve and present data as information, since information for FDA submissions is the most important by-product of our R & D processes. Information management is pivotal to our success in convincing regulators that our product candidates are suitable for marketing. Through our use of information technologies and our experience in maintaining records important to us and to FDA, we are well-qualified to comment on *The Draft Guidance for Industry, Electronic Records: Electronic Signatures, Maintenance of Electronic Records* (hereafter referred to as *The Draft Guidance on Part 11-Records Maintenance*).

**General Comment**

We appreciate the opportunity to review *The Draft Guidance on Part 11-Records Maintenance* and to share our comments on this important topic. Through continued dialogue with regulators on Part 11 issues, we strive to achieve clarity in certain requirements for those subject to the regulation and to promote reasonable expectations of what is achievable for

00D-1539

C8

regulators, ultimately leading to a better mutual understanding of what is practical for compliance.

### **Specific Comments**

#### **Section 5.1 Procedures For Electronic Records Maintenance Should Be Established and Followed;**

And,

#### **Section 5.3 Continued Availability and Readability of Electronic Record Information Should Be Ensured**

These sections of *The Draft Guidance on Part 11-Records Maintenance* address procedures and controls required for the maintenance of records “to enable their accurate and ready retrieval throughout the records retention period.”<sup>1</sup> These sections recommend implementation of a technical approach to long-term electronic record storage (Section 5.1) and periodic assessment of a representative number of records to assure that record contents “can still be read throughout the retention period”<sup>2</sup> (Section 5.3). However, we are unaware of any technology for the long-term archival of electronic records that can remain available over the record retention period.

Recommendation 1: *The Draft Guidance on Part 11-Records Maintenance* should reflect this state-of-the-art detail and permit either an alternate procedural or a technical approach for records retrieval.

Recommendation 2: With reference to periodic assessments, *The Draft Guidance on Part 11-Records Maintenance* should allow establishment and validation of duration periods of the various media as an alternative to periodic checks of the records stored on the media.

#### **Section 5.4 Electronic Records Should Be Stored Under Appropriate Environmental Conditions**

Operating variables such as temperature and humidity can be monitored by a Building Automation System (BAS) or manually *via* a chart recorder. However, dust, vibration and sources of electromagnetic and radio frequency interference cannot be easily monitored with any existing BAS. We agree with FDA’s assessment that “producers and suppliers of recording media can be a good source of information about specifications and precautions regarding such factors as temperature, humidity, dust, vibration, and sources of electromagnetic and radio frequency interference.”<sup>3</sup> Supplier specifications and precautions should always be considered during installation of a system.

Recommendation 3: *The Draft Guidance on Part 11-Records Maintenance* should recommend on-going monitoring, specifically of temperature and humidity conditions, of the environment in which electronic records are stored in order to limit the compliance

---

<sup>1</sup> Lines 199-200, *Draft Guidance for Industry, 21 CFR Part 11; Electronic Signatures, Maintenance of Electronic Records*

<sup>2</sup> Lines 228-229, *Draft Guidance for Industry, 21 CFR on Part 11; Electronic Signatures, Maintenance of Electronic Records*

<sup>3</sup> Lines 251-254, *Draft Guidance for Industry, 21 CFR on Part 11; Electronic Signatures, Maintenance of Electronic Records*

requirement to what is feasible. There should be no expectation that the other factors would be actively monitored.

**Section 5.5 Ability To Process An Electronic Record's Information Throughout Its Records Retention Period Should Be Preserved; and,**

**Section 6.2.1.4 The Electronic Records Migration Approach -The Ability To Process Information In Electronic Records Should Be Preserved**

The requirement to maintain processing capability for an old system is a substantial extension of the scope of 21 CFR Part 11, Subpart B 11.10(b). Acceptable alternatives are addressed in the predicate rules and should be retained in *The Draft Guidance on Part 11-Records Maintenance*. For example, the Good Manufacturing Practices (GMP) regulations<sup>4</sup> and the Good Laboratory Practices (GLP) regulations<sup>5</sup> both state:

“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.”

These are examples of methods to retain information that do not require reprocessing capability.

Recommendation 4: The requirement to maintain a capability to “process” information throughout its retention period should be replaced with alternate language from the GMP or GLP regulations, from which this requirement is derived. Language, such as the following, is well-understood and would be suitable if reproduced from the Part 11 regulation in *The Draft Guidance on Part 11-Records Maintenance*:

“Throughout the records retention period, the electronic record should be maintained in a manner that allows the electronic record's information to generate copies in human and computer readable form that are suitable for FDA inspection, review, and copying.”<sup>6</sup>

**Section 6.2.1.3 The Electronic Records Migration Approach - Electronic Record Integrity Attributes Should Be Preserved**

This Section of *The Draft Guidance on Part 11-Records Maintenance* requires insertion of a record of migration into the migrated audit trail. Since the migration from an old system to a new system is a documented change control process, and the new system will be validated appropriately, documentation of the migration event in an audit trail is an unnecessary step. Furthermore, this is not typically supported by commercial software and would be very costly to program individually.

Recommendation 5: The requirement to insert a record of migration into the migrated audit trail provides unnecessary redundancy and should be deleted.

---

<sup>4</sup> GMPs @ 21 CFR 211.180 (d)

<sup>5</sup> GLPs @ 21 CFR 58.195 (g)

<sup>6</sup> 21 CFR 11.10(b)

**Section 6.2.1.5 Unavoidable Differences And Losses Should Be Accounted For And Explained In The Migrated Electronic Record Or New System Documentation**

*The Draft Guidance on Part 11-Records Maintenance* provides a specific example for verification of the migration of digital signatures, using a 3<sup>rd</sup> party to verify the digital signature in the old system prior to migration. In this example, the 3<sup>rd</sup> party applies a new “notarized” digital signature in the new system attesting to the authenticity of the original digital signature that can no longer be verified in the new system.

Recommendation 6: An alternate approach, recommended by the National Archives and Records Administration (NARA) in its guidance to Federal Agencies on implementing electronic signatures, should be considered for inclusion in *The Draft Guidance on Part 11-Records Maintenance*. NARA recommends maintaining “adequate documentation of the records” validity, such as trust verification records gathered at or near the time of record signing. Language similar to the following NARA recommendation would be useful and consistent with current practices.

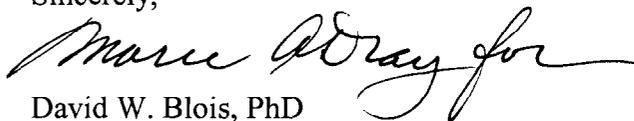
“Maintaining adequate documentation of validity gathered at or near the time of record signing may be preferable for records that have permanent or long-term retentions since it is less dependent on technology and much more easily maintained as technology evolves over time.”<sup>7</sup>

**Conclusion**

Specific recommendations provided here, if adopted, will clarify certain ambiguities in the document and, thereby, allow greater understanding of requirements by all concerned, with the objective of improving compliance. In some cases, there are interpretations of key requirements within this *Draft Guidance* that deviate from the originating regulations. In those cases, sponsors who must comply will defer to the regulations, which are legally binding. Therefore, strict adherence to the regulations in interpreting certain controversial provisions within this *Draft Guidance* should be observed.

We appreciate your consideration of our comments on these important issues.

Sincerely,



David W. Blois, PhD  
Senior Vice President  
Global Regulatory Policy

<sup>7</sup> *Records Management Guidance For Agencies Implementing Electronic Signature Technologies*, National Archives and Records Administration (NARA), October 18, 2002, Page 8, Para. 2, line 1 (Section 4.3)