



2004N-0133

E. Edward Kavanaugh  
President

July 9, 2004

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Re: Electronic Record; Electronic Signatures; Public Meeting  
Docket No. 2004N-0133

Dear Sir or Madam:

These comments are submitted on behalf of The Cosmetic, Toiletry, and Fragrance Association (CTFA)<sup>1</sup> in response to the Food and Drug Administration's (FDA) announcement of a public meeting to discuss various topics concerning regulations on electronic records and electronic signatures in 21 CFR Part 11.

In the Federal Register of April 8, 2004, FDA announced that it planned to hold a public meeting scheduled for June 11, 2004 in Washington, DC.<sup>2</sup> In announcing the public meeting, FDA provided background information explaining that 21 CFR Part 11 provides the criteria under which FDA considers electronic records, electronic signatures, and handwritten signatures executed to electronic records as equivalent to paper records and handwritten signatures executed on paper. These regulations were originally intended to permit the widest possible use of electronic technology, consistent with FDA's responsibility to protect the public health. However, after the Part 11 regulations were implemented in 1997, concerns were raised that some interpretations of Part 11 by FDA would (1) unnecessarily restrict the use of electronic technology in a manner

---

<sup>1</sup>CTFA is the national trade association representing the personal care product industry. Founded in 1894, CTFA represents almost 600 companies involved in the sale or distribution of cosmetics, toiletries, fragrances and OTC drugs throughout the world. CTFA represents the manufacturers or distributors of the vast majority of those products sold in the United States. Approximately one-half of CTFA's members are manufacturers or distributors of finished personal care products. The other one-half are suppliers of goods or services to those manufacturers or distributors.

<sup>2</sup>Although the public meeting was cancelled because of the death of President Reagan, FDA noted that all comments and presentations should be submitted to docket number 2004N-0133 by July 9, 2004, for consideration by the Agency.

2004N-0133

C26

inconsistent with FDA's stated intent in issuing the rule, (2) significantly increase the costs of compliance to an extent that was not contemplated at the time the rule was drafted, and (3) discourage innovation and technological advances without providing a significant public health benefit. These concerns focused primarily on Part 11 requirements for validation, audit trails, record retention, record copying, and legacy systems.

FDA has noted that its re-examination of Part 11 is an outgrowth of the agency's broader initiative to implement a risk-based approach to pharmaceutical cGMPs for the 21st century. Further, FDA stated in the guidance for industry entitled "Part 11, Electronic Records; Electronic Signatures--Scope and Application" that was issued on September 5, 2003 (68 FR 52779), that the agency anticipated rulemaking to change Part 11 as a result of this re-examination. At the same time, FDA noted that it intended to continue to enforce all predicate rule requirements which are the underlying requirements set forth in the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and FDA regulations (other than Part 11).

In the April 8, 2004 announcement, the agency described its objectives to include the following:

- To prevent unnecessary controls and costs, yet retain the objectives of the rule.
- To clarify the scope of Part 11 (e.g., how it relates to other FDA regulations).
- To ensure that Part 11 provides an adequate level of record security, authenticity, and integrity, and encourages innovation and technological advances.

To further these objectives, the agency stated that it intended to accomplish the following:

- Identify areas where Part 11 could be less prescriptive and detailed, and
- Clarify the relationship between Part 11 and other FDA regulations (predicate rules) with respect to record and recordkeeping requirements.

In the announcement of the public meeting, the agency invited discussion on the scope of Part 11, risk-based approaches, validation, audit trails, record retention, record copying, and legacy systems and identified specific issues and questions for comment.

The agency also posed additional questions for comment, including:

1. What are the economic ramifications of modifying Part 11 based on the issues raised in this document?
2. Is there a need to clarify in Part 11 which records are required by predicate rules where those records are not specifically identified in predicate rules? If so, how could this distinction be made?
3. In what ways can Part 11 discourage innovation?
4. What potential changes to Part 11 would encourage innovation and technical

- advances consistent with the agency's need to safeguard public health?
5. What risk-based approaches would help to ensure that electronic records have the appropriate levels of integrity and authenticity elements and that electronic signatures are legally binding and authentic?
  6. The Part 11 guidance announced that the agency would exercise enforcement discretion (during our re-examination of Part 11) with respect to all Part 11 requirements for systems that otherwise were operational prior to August 20, 1997 (legacy systems), the effective date of Part 11. What are stakeholder concerns in regards to modifications made to legacy systems in use as of August 1997? Can the use of risk mitigation and appropriate controls eliminate concerns regarding legacy systems?
  7. Should Part 11 address record conversion?
  8. Are there provisions of Part 11 that should be augmented, modified, or deleted as a result of new technologies that have become available since Part 11 was issued?

Although many of the products of CTFA members are regulated solely as cosmetics and are not affected by this proposal, a very significant number of our members' products are regulated both as cosmetics and as over-the-counter (OTC) drugs. These products, referred to as "cosmetic-drugs" in this document, claim and provide both a cosmetic and a drug benefit. Both such benefits are highly valued by consumers. Products within this category include, but are not limited to, (1) antidandruff shampoos, (2) antiperspirant/deodorants, (3) skin protectants, (4) antimicrobial soaps (healthcare antiseptic drug products) and (5) sunscreens, including many traditional cosmetic products such as skin-care products, foundations and lipsticks that contain sunscreens.

For the past 30 years CTFA has actively participated in addressing both the scientific and regulatory issues involved with developing OTC monographs for all product categories that include cosmetic-drug products. For each of these rulemakings, CTFA has filed numerous written comments with FDA, focusing on many of the unique issues facing cosmetic-drug products.

Cosmetic-drugs include many products where there is no dose limitation. Dosage limitations are typical for most regulated drugs that are not also cosmetics. The absence of an overall dosage limitation for cosmetic-drugs is reflective of the inherently wide safety margins (i.e., the difference between the effective dose and a toxic dose is relatively large) associated with the use of such products. For the purpose of differentiating between dose-limited and non-dose-limited drugs, CTFA has proposed in past submissions to define "dosage limitation" as follows:<sup>3</sup>

---

<sup>3</sup>See comments by The Cosmetic, Toiletry, and Fragrance Association on the Food and Drug Administration's Proposed Regulations on Over-The-Counter Drug Labeling, 62 Federal Register 9024 (February 27, 1997) dated October 6, 1997, p. 3.

“a set of limitations on the size, frequency, and number of doses required in the labeling of a product marketed either pursuant to a Tentative Final Monograph, where applicable, or Final Monograph for an OTC Drug Product Category or a specific New Drug Application approval.”

It should be noted that the cosmetic-drugs listed above are regulated in most other countries as cosmetics even though they are functionally identical to those marketed in the United States. Supporting industry's contention that the increased regulatory oversight required in the U.S. for such products is largely unnecessary, particularly as that oversight is embodied in Part 11.

CTFA is a member of the Industry Coalition on Part 11 that has been working with FDA on Part 11 issues. The Coalition is made up of 14 trade associations representing manufacturers of FDA-regulated products including foods, drugs, cosmetics, veterinary drugs, and medical devices. CTFA notes that comments have been submitted by the Part 11 Coalition, and we fully support those comments. Further, CTFA will continue to collaborate with this group as the specifics of the Part 11 requirements are discussed and clarified. CTFA submitted comments to the Part 11 docket on April 28, 2003 and is submitting these comments supplemental to those submitted by the Coalition.

In considering the comments filed by the Coalition, CTFA agrees that both the preamble and the regulation itself are too prescriptive and that FDA attempted to pre-determine the movement of technology, rather than permit technology to evolve naturally to address the issues related to security and authenticity of electronic records. We both agree that a technology neutral approach that is enabling is preferable. CTFA strongly agrees that any regulation issued must be revised to permit the use of a risk assessment for such controls as validation, audit trails and record retention and that such an approach should look at endpoints that focus on product quality and safety. There should also be a direct linkage to the predicate rules, acknowledging that a record is a record regardless of its format (regulations should not distinguish between paper and electronic versions). CTFA also strongly supports the Coalition recommendation that industry not be limited and should be permitted to apply a risk-based approach to all areas of Part 11 and that companies should be able to select, develop and document the appropriate approach for their organization.

CTFA adds that the agency should clearly allow alternative approaches or exclusions for products that are of very low risk - such as the cosmetic-drug products that are not dose-limited. (In fact, there is a strong argument that Part 11 regulations are not necessary and that the predicate rules alone are sufficient.) For inherently low risk products like cosmetic-drugs, systems can be designed that ensure safety and efficacy without requiring the level of control that characterizes prescription drugs. For example, manufacturers of non-dose-limited OTC drug-cosmetics can focus on the critical points in the manufacturing process that are most directly relevant to ensuring the safety,

efficacy and quality of the product. The design of the record-keeping system would be defined by the selected critical stages in manufacturing. For example, application of this approach to a sunscreen OTC cosmetic-drug product may focus on final product analysis to ensure that the set levels of sunscreen active ingredients are achieved and that the proper inactive (cosmetic) ingredients are in the formulation. Record keeping requirements subject to the drug cGMPs and Part 11 would be applied only to certain select points in the manufacturing process. This approach can effectively ensure safety and efficacy, taking into account the inherent low risk presented by this product category. Advanced technology, such as in-line monitoring and analysis, could be applied on a wider scale.

In considering the specific questions posed by FDA, CTFA is especially concerned about the economic ramifications of applying Part 11 without taking into consideration the inherent risk posed by the product. Compliance with the full requirements of Part 11, as they are applied for dose-limited OTC or prescription drugs, represents a significant economic burden on the manufacturers of cosmetic-drugs. Less costly approaches can be employed that will equally serve to ensure safety and efficacy. Further, on a broader scale, a more flexible approach would serve to "encourage innovation and technical advances consistent with the agency's need to safeguard public health." (question 4 above). Also, as asked in question 5, CTFA feels that the recognition of alternative approaches to meeting the requirements of Part 11, based on the application of systems that take into account risk, would ensure that electronic records have the appropriate levels of integrity and authenticity elements and that electronic signatures are legally binding and authentic commensurate with that risk.

### Recommendations

CTFA supports the initiative taken by FDA to re-examine the Part 11 regulations and to apply a risk-based approach to cGMPs. FDA has stated that the same requirements are not appropriate and necessary for all drug products and that safety and efficacy can be achieved through different levels of oversight based on a risk assessment. The manufacturers of cosmetic-drugs can assume a greater level of responsibility and flexibility in designing systems to ensure the safety and efficacy of their products. The application of a cGMP system that is appropriate for prescription or dose-limited OTC drugs is not needed for non-dose limited cosmetic drugs.

We ask that FDA take the following actions in revising the regulations in 21 CFR Part 11 and in applying a risk-based approach to cGMPs for cosmetic-drugs:

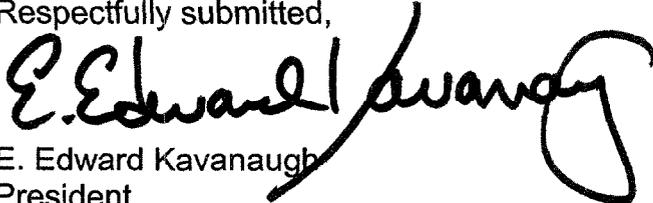
- (1) FDA should acknowledge that cosmetic-drugs present a clear low risk and do not present a risk that would require the same level or type of oversight that is applied to drugs that are dose restricted or that have a narrow therapeutic margin.

- (2) Guidance and regulations developed by FDA should clearly acknowledge the low risk of these products and build in the flexibility that allows the use of alternative approaches to meeting the intent of the cGMP regulations.
- (3) FDA should state that alternative approaches for applying Part 11 requirements and cGMPs can be used for cosmetic-drugs so that they are not subject to unnecessary and costly systems that are applied to traditional drugs.
- (4) FDA investigators should be trained to take into account the intrinsic low risk for these products during cGMP inspections.

The development of alternative approaches should allow individual manufacturers to develop and apply their own systems for ensuring the safety and efficacy of cosmetic-drug products.

CTFA appreciates the opportunity to provide these comments and looks forward to working with the agency to explore regulatory approaches to cosmetic-drugs that are more aligned with their risk. Please feel free to contact us if you have questions or need additional information.

Respectfully submitted,



E. Edward Kavanaugh  
President

cc: Steven K. Galson, M.D. (HFD-1)  
Joseph Famulare (HFD-320)  
Yonca Bull, M.D. (HFD-105)  
Charles Ganley, M.D. (HFD-560)  
Robert Brackett, Ph. D. (HFS-1)  
Linda M. Katz, M.D. (HFS-100)