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Consumer Federation of America

July 23, 1998

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive, rm. 1-23
Rockville, MD 20857

Dissemination of Information on Unapproved/New Uses for Marketed Drugs, Biologics, and Devices; Docket No. 98 N-0222

To Whom It May Concern:

The Consumer Federation of America urges the Food and Drug Administration to enact strong regulations governing the dissemination of information related to unapproved and new uses of marketed drugs, biologics and devices. The adoption of the off-label provisions followed a negotiated compromise which included a system of "safeguards". The insertion of the sunset provision is proof of the controversy. There is virtually no legislative history, and the statute language is prescriptive, leaving little to FDA interpretation. In general, we think the FDA has acted correctly here to protect public health and safety.

CFA opposed last year's Food and Drug Administration Modernization Act (FDAMA). Among other concerns, we were distressed by the lowering of the efficacy standard and the adoption of Sec. 401 [codified as Sec. 551], allowing off-label promotion. Separately and together, we believe they will allow millions of Americans to use products whose safety and effectiveness has not been thoroughly established.

CFA is also a signatory to comments in this Docket filed with other patient and consumer organizations. Those comments are incorporated herein by reference. We offer the following additional comments.

Information that may be disseminated Sec 99.101

First, the definition of "scientifically sound" is within the FDA's discretion, subject to an "arbitrary or capricious" standard. It is important that the FDA give unambiguous direction to industry, as it has done so here.

More to the point, based on our discussions with experts, what the FDA is requiring here is nothing more than the standard format for articles in peer-reviewed literature. The attached page from the Journal of the American Medical Association's Instructions to Authors bears this out.

Further, the medical journal editor who spoke at the public hearing did not indicate concern about the proposed definition, but welcomed clear guidance from the FDA. With the passage of FDAMA, we are entering a new paradigm in drug testing and marketing. Is there any doubt that there will be increased incentive get the results of clinical investigations published quickly? To the extent that journals on the Index Medicus do not require such disclosures in articles, they should.

At least in the case of health care practitioners, this information needs to be included in the article for a fair evaluation. Under the usual time constraints, it is both unrealistic and unfair to expect a practitioner to independently track it down.

Mandatory statements and information Sec. 99.103

There is little opportunity for FDA interpretation here.

The factors listed for consideration in determining whether a statement is "prominently displayed" do not dictate a particular format, but serve notice that valuable information cannot be buried or downplayed by clever packaging.

There should be no confusion about what is required of manufacturers. More important, recipients of the information should not be confused. This can best be accomplished by an up-front, consistent [in terms of wording] notice of the off-label nature of the use being promoted.

Economically prohibitive supplements Sec 99.205

It is up to the FDA to define "economically prohibitive". It must give consistent and clear construction while not allowing the exceptions to become the rule. This is an area fraught with controversy. What does it really cost to conduct studies?

We believe that the FDA has given a fair construction of the word "prohibitive". After all, Congress did not say economically "difficult" or "practical". Given the indefinite nature of this exemption, it should only be used in the rarest of circumstances.

CFA supports requiring the report of an independent certified public accountant

instead of manufacturer attestation. This will ensure some level of due diligence in reviewing cost estimates and, presumably, less pressure to inflate the numbers.

Manufacturer statements and certifications

In several sections [99.201, 99.203, 99.205, 99.303], the manufacturer is required to submit a statement or other documents to the FDA. CFA recommends that all such statements, certifications and documents be certified by an officer from the manufacturer's executive committee.

The risks associated with off-label dissemination are great, and we expect high public scrutiny. Senior management must be vested in the process and must not be able to evade public responsibility downstream.

Recordkeeping and reports

CFA urges that in ALL cases, manufacturers be required to keep records identifying individual recipients of the disseminated information. Short of that, there is no guarantee that timely and decisive corrective action can be taken in the event of a serious adverse effect. Cessation of dissemination is not the critical issue, it is notification of those already at risk. Without the ability to notify practitioners, there is less chance of success.

Presumably, off-label dissemination is not meant to circumvent FDA review and should be limited in scope. Therefore, any recordkeeping burden is outweighed, at least in the short term, by the risk presented and the need to make off-label dissemination work safely.

Request for clarification

Finally, we seek clarification under Sees 99.201 (a) and 99.501 (b)(3) that a manufacturer must submit any additional article or publication to the FDA for 60-day review before it can be disseminated. While we think it clear from 99.201, that this is the case, there should be no room for argument under section 99.501 that making the semiannual filing is sufficient once the manufacturer has received the initial approval to disseminate information about a particular use.

Respectfully submitted,



Mary Rouleau
Legislative Director

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**DOCKET
98N-0222**

**ON
FDAMA SECTION 401 DISSEMINATION OF INFORMATION ON UNAPPROVED/NEW USES**

**Comment 22
"JAMA Instructions for Authors, Manuscript Criteria information," JAMA January 7, 1998, Vol. 279,
No. 1**

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