

(5) Not be derived from clinical research conducted by another manufacturer unless the manufacturer disseminating the information has the permission of such other manufacturer to make the dissemination.

(b) For purposes of this part:

(1) FDA will find that all journal articles and reference publications (as those terms are defined in §99.3) are scientifically sound except:

(i) Letters to the editor;

(ii) Abstracts of a publication;

(iii) Those regarding Phase 1 trials in healthy people;

(iv) Flagged reference publications that contain little or no substantive discussion of the relevant clinical investigation; and

(v) Those regarding observations in four or fewer people that do not reflect any systematic attempt to collect data, unless the manufacturer demonstrates to FDA that such reports could help guide a physician in his/her medical practice.

(2) A reprint or copy of an article or reference publication is “unabridged” only if it retains the same appearance, form, format, content, or configuration as the original article or publication. Such reprint, copy of an article, or reference publication shall not be disseminated with any information that is promotional in nature. A manufacturer may cite a particular discussion about a new use in a reference publication in the explanatory or other information attached to or otherwise accompanying the reference publication under §99.103.

§99.103 Mandatory statements and information.

(a) Any information disseminated under this part shall include:

(1) A prominently displayed statement disclosing:

(i) For a drug, “This information concerns a use that has not been approved by the Food and Drug Administration.” For devices, the statement shall read, “This information concerns a use that has not been approved or cleared by the Food and Drug Administration.” If the information to be disseminated includes both an approved and unapproved use or uses or a cleared and uncleared use or uses, the manufacturer shall modify the statement to

identify the unapproved or uncleared new use or uses. The manufacturer shall permanently affix the statement to the front of each reprint or copy of an article from a scientific or medical journal and to the front of each reference publication disseminated under this part;

(ii) If applicable, the information is being disseminated at the expense of the manufacturer;

(iii) If applicable, the names of any authors of the information who were employees of, or consultants to, or received compensation from the manufacturer, or who had a significant financial interest in the manufacturer during the time that the study that is the subject of the dissemination was conducted up through 1 year after the time the article/reference publication was written and published;

(iv) If applicable, a statement that there are products or treatments that have been approved or cleared for the use that is the subject of the information being disseminated; and

(v) The identification of any person that has provided funding for the conduct of a study relating to the new use of a drug or device for which such information is being disseminated; and

(2) The official labeling for the drug or device;

(3) A bibliography of other articles (that concern reports of clinical investigations both supporting and not supporting the new use) from a scientific reference publication or scientific or medical journal that have been previously published about the new use of the drug or device covered by the information that is being disseminated, unless the disseminated information already includes such a bibliography; and

(4) Any additional information required by FDA under §99.301(a)(2). Such information shall be attached to the front of the disseminated information or, if attached to the back of the disseminated information, its presence shall be made known to the reader by a sticker or notation on the front of the disseminated information and may consist of:

(i) Objective and scientifically sound information pertaining to the safety or effectiveness of the new use of the drug or device and which FDA determines is

necessary to provide objectivity and balance. This may include information that the manufacturer has submitted to FDA or, where appropriate, a summary of such information and any other information that can be made publicly available; and

(ii) An objective statement prepared by FDA, based on data or other scientifically sound information, bearing on the safety or effectiveness of the new use of the drug or device.

(b) Except as provided in paragraphs (a)(1)(i) and (a)(4) of this section, the statements, bibliography, and other information required by this section shall be attached to such disseminated information.

(c) For purposes of this section, factors to be considered in determining whether a statement is “prominently displayed” may include, but are not limited to, type size, font, layout, contrast, graphic design, headlines, spacing, and any other technique to achieve emphasis or notice. The required statements shall be outlined, boxed, highlighted, or otherwise graphically designed and presented in a manner that achieves emphasis or notice and is distinct from the other information being disseminated.

§ 99.105 Recipients of information.

A manufacturer disseminating information on a new use under this part may only disseminate that information to a health care practitioner, a pharmacy benefit manager, a health insurance issuer, a group health plan, or a Federal or State Government agency.

Subpart C—Manufacturer’s Submissions, Requests, and Applications

§ 99.201 Manufacturer’s submission to the agency.

(a) Sixty days before disseminating any written information concerning the safety, effectiveness, or benefit of a new use for a drug or device, a manufacturer shall submit to the agency:

(1) An identical copy of the information to be disseminated, including any information (e.g., the bibliography) and statements required under § 99.103;

(2) Any other clinical information which the manufacturer has relat-

ing to the effectiveness of the new use, any other clinical trial information that the manufacturer has relating to the safety of the new use, any reports of clinical experience pertinent to the safety of the new use, and a summary of such information. For purposes of this part, clinical trial information includes, but is not limited to, published papers and abstracts, even if not intended for dissemination, and unpublished manuscripts, abstracts, and data analyses from completed or ongoing investigations. The reports of clinical experience required under this paragraph shall include case studies, retrospective reviews, epidemiological studies, adverse event reports, and any other material concerning adverse effects or risks reported for or associated with the new use. If the manufacturer has no knowledge of clinical trial information relating to the safety or effectiveness of the new use or reports of clinical experience pertaining to the safety of the new use, the manufacturer shall provide a statement to that effect;

(3) An explanation of the manufacturer’s method of selecting the articles for the bibliography (e.g., the databases or sources and criteria (i.e., subject headings/keywords) used to generate the bibliography and the time period covered by the bibliography); and

(4) If the manufacturer has not submitted a supplemental application for the new use, one of the following:

(i) If the manufacturer has completed studies needed for the submission of a supplemental application for the new use:

(A) A copy of the protocol for each completed study or, if such protocol was submitted to an investigational new drug application or an investigational device exemption, the number(s) for the investigational new drug application or investigational device exemption covering the new use, the date of submission of the protocol(s), the protocol number(s), and the date of any amendments to the protocol(s); and

(B) A certification stating that, “On behalf of [insert manufacturer’s name], I certify that [insert manufacturer’s name] has completed the studies needed for the submission of a supplemental application for [insert new use] and will submit a supplemental application