

(h) *Pharmacy benefit manager* means a person or entity that has, as its principal focus, the implementation of one or more device and/or prescription drug benefit programs.

(i) A *reference publication* is a publication that:

(1) Has not been written, edited, excerpted, or published specifically for, or at the request of, a drug or device manufacturer;

(2) Has not been edited or significantly influenced by such a manufacturer;

(3) Is not solely distributed through such a manufacturer, but is generally available in bookstores or other distribution channels where medical textbooks are sold;

(4) Does not focus on any particular drug or device of a manufacturer that disseminates information under this part and does not have a primary focus on new uses of drugs or devices that are marketed or are under investigation by a manufacturer supporting the dissemination of information; and

(5) Does not present materials that are false or misleading.

(j) *Scientific or medical journal* means a scientific or medical publication:

(1) That is published by an organization that has an editorial board, that uses experts who have demonstrated expertise in the subject of an article under review by the organization and who are independent of the organization, to review and objectively select, reject, or provide comments about proposed articles, and that has a publicly stated policy, to which the organization adheres, of full disclosure of any conflict of interest or biases for all authors or contributors involved with the journal or organization;

(2) Whose articles are peer-reviewed and published in accordance with the regular peer-review procedures of the organization;

(3) That is generally recognized to be of national scope and reputation;

(4) That is indexed in the Index Medicus of the National Library of Medicine of the National Institutes of Health; and

(5) That is not in the form of a special supplement that has been funded in whole or in part by one or more manufacturers.

(k) *Supplemental application* means:

(1) For drugs, a supplement to support a new use to an approved new drug application;

(2) For biologics, a supplement to an approved license application;

(3) For devices that are the subject of a cleared 510(k) submission and devices that are exempt from the 510(k) process, a new 510(k) submission to support a new use or, for devices that are the subject of an approved premarket approval application, a supplement to support a new use to an approved premarket approval application.

Subpart B—Information to be Disseminated

§ 99.101 Information that may be disseminated.

(a) A manufacturer may disseminate written information concerning the safety, effectiveness, or benefit of a use not described in the approved labeling for an approved drug or device or in the statement of intended use for a cleared device, provided that the manufacturer complies with all other relevant requirements under this part. Such information shall:

(1) Be about a drug or device that has been approved, licensed, or cleared for marketing by FDA;

(2) Be in the form of:

(i) An unabridged reprint or copy of an article, peer-reviewed by experts qualified by scientific training or experience to evaluate the safety or effectiveness of the drug or device involved, which was published in a scientific or medical journal. In addition, the article must be about a clinical investigation with respect to the drug or device and must be considered to be scientifically sound by the experts described in this paragraph; or

(ii) An unabridged reference publication that includes information about a clinical investigation with respect to the drug or device, which experts qualified by scientific training or experience to evaluate the safety or effectiveness of the drug or device that is the subject of the clinical investigation would consider to be scientifically sound;

(3) Not pose a significant risk to the public health;

(4) Not be false or misleading. FDA may consider information disseminated under this part to be false or misleading if, among other things, the information includes only favorable publications when unfavorable publications exist or excludes articles, reference publications, or other information required under § 99.103(a)(4) or the information presents conclusions that clearly cannot be supported by the results of the study; and

(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