Biologic, or Antibiotic Drug for Human Use, for use in accordance with part 601 (21 CFR part 601), by applicants for licenses for specified biotechnology and specified synthetic biological products. In the final rule, ''Elimination of Establishment License Application for Specified Biotechnology and Specified Synthetic Biological Products,'' published elsewhere in this issue of the Federal Register, FDA is amending § 601.2 (a) and adding new § 601.2 (c) to create a licensing scheme for specified biotechnology and specified synthetic biological products. The final rule requires an applicant seeking marketing approval for specified biotechnology and specified synthetic biological products to submit a single biologics license application to CBER. FDA Form 3439 has received interim approval from OMB for use by applicants subject to the above-referenced final rule.

In the November 1995 report entitled, ''Reinventing the Regulation of Drugs Made from Biotechnology'' report, the President and Vice-President announced a series of regulatory reform initiatives, including FDA's intention to use a single harmonized application form for all licensed biological products and all drug products. The harmonized form will be made available for public comment and submitted to OMB for review and approval. FDA also intends to develop guidance to assist applicants in completing the harmonized application. Once it is approved for use by OMB, the harmonized form will supersede FDA Form 3439. Until that time, applicants for licenses for specified biotechnology and specified synthetic biological products may use the interim FDA Form 3439.

Under the Paperwork Reduction Act of 1995 (Pub. L. 104–13), all forms requesting a collection of information on identical items from 10 or more public respondents must be approved by OMB and must display a valid OMB control number and expiration date. FDA Form 3439 was approved under OMB control number 0910–0316. The expiration date for the form is December 31, 1997.

Dated: May 9, 1996.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 96–12145 Filed 5–10–96; 10:13 am]

BILLING CODE 4160–01–F

[Docket No. 95N–0227]

Direct-to-Consumer Promotion

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is publishing a notice making clear that the agency does not require preclearance of prescription product promotion (advertising and promotional labeling) of human or animal drugs, biologics, or restricted medical devices directed toward consumers. FDA is also requesting comments on its intent to consider certain FDA-approved patient labeling as adequate to fulfill the brief summary requirement in consumer-directed advertisements. Finally, FDA is soliciting comments concerning several issues related to consumer-directed promotion of prescription biologics, human and animal drugs, and restricted medical devices to help guide policy decisions.

DATES: Written comments by August 12, 1996.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Nancy M. Ostrove, Division of Drug Marketing, Advertising and Communications (HFD–40), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, rm. 17–B04, Rockville, MD 20857, 301–827–2828, or via Internet at Ostrove@cder.fda.gov.

SUPPLEMENTARY INFORMATION:

I. Background

Under the Federal Food, Drug, and Cosmetic Act (act) and the Public Health Service Act, the Food and Drug Administration (FDA) has responsibility for regulating the labeling and advertising of prescription drugs (animal and human), biologics, and restricted medical devices. Labeling and advertising must follow certain requirements, as defined by the Act and implementing regulations.

Under section 502(n)of the act (21 U.S.C. 352(n)), an advertisement for a prescription drug must contain, in addition to the product's established name and quantitative composition, ''such other information in brief summary relating to side effects, contraindications, and effectiveness * * *.'' This requirement is further defined in prescription drug advertising regulations at § 202.1(e) (21 CFR 202.1(e)). Under section 502(r) of the act (21 U.S.C. 352(r)), an advertisement for a restricted medical device must contain, in addition to the established name, ''a brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and contraindications * * *.''

The act and FDA's advertising regulations do not distinguish between targeted audiences. FDA recognizes, however, that there are differences between the information needs of health care professionals and consumers resulting from differences in medical and pharmaceutical expertise, and differences in roles as potential recipients of medications or prescribers of medications, that may affect their perceptions, comprehension, and interpretation of promotional claims. In light of these differences, FDA is continuing to evaluate its policies and regulations.

In the Federal Register of August 16, 1995 (60 FR 42581), FDA announced a part 15 (21 CFR part 15) hearing to be held on October 18 and 19, 1995. In that document, the agency solicited oral testimony and written responses to a series of questions concerning direct-to-consumer (DTC) promotion of prescription drugs. At the hearing, the agency heard testimony from representatives of consumer and patient groups, advertising associations, and foreign governments, as well as from individual academicians, attorneys, marketers, and pharmaceutical manufacturers. The agency accepted written comments until December 29, 1995. FDA is currently evaluating the testimony, comments, and issues raised by both the public hearing and citizen petitions submitted prior to the hearing.

While this evaluation proceeds, FDA is providing clarification of two of its policies and soliciting additional information to help in the development of overall policy. FDA views these efforts as part of a comprehensive process designed to encourage meaningful communication to consumers about prescription drugs, biologics, and restricted medical devices, while continuing to help ensure that consumers are adequately protected from false, misleading or otherwise violative promotion.

II. Preclearance

One issue raised in oral testimony, written comments, and citizen petitions was an objection to the perceived requirement for manufacturers to obtain prior clearance from the agency for all prescription drug and biological DTC promotion. There is, in fact, no such requirement. Given public and congressional concern since the early 1980's about prescription drug DTC promotion, together with the inexperience of the pharmaceutical industry in producing DTC advertising, FDA had informally requested manufacturers to submit, on a voluntary basis, proposed DTC promotional

labeling and advertising for review and comment prior to use. See § 202.1(j)(4), which provides that ''any advertisement may be submitted to the Food and Drug Administration prior to publication for comment.''

FDA wishes to clarify that it has never required preclearance of consumer-directed prescription drug promotion, or advertising for restricted devices. Under sections 502(n) and 502(r) of the act, FDA may require prior approval of prescription drug and medical device advertisements only in ''extraordinary circumstances.'' (See, e.g., § 202.1(j)(1)—prior approval will be required when a sponsor or FDA receives information, not widely publicized in medical literature, that a drug may cause fatalities or serious injuries, and despite notification from FDA, the sponsor fails to publicize adequately such information.)

FDA believes that industry's desire for agency guidance on proposed DTC promotion and applicable regulatory requirements, and the cost of developing corrective materials or campaigns explains the high rate of submission of DTC promotional materials for prior review and comment. However, it appears that the agency's request that manufacturers voluntarily obtain advice on proposed DTC materials has been misinterpreted as a requirement. FDA reiterates that it does not now require, nor has it ever required, manufacturers to submit DTC promotional labeling and advertising for preclearance. [1]

III. Patient Labeling in Fulfillment of the ''Brief Summary'' Requirement

FDA recognizes that many consumers do not have the technical background to understand fully the information typically included in prescription drug and biological advertisements to fulfill the ''brief summary'' requirement. To meet the ''brief summary'' requirement, sponsors typically reprint, in small type, whole sections of the professional labeling, which is generally written in terms that are not easily understood by the average consumer.

Some prescription drugs and biological products have FDA-approved labeling, in addition to that written for health professionals, that contains information intended to be understandable to patients. This patient labeling contains information that comprehensively, although not exhaustively, describes the safety and efficacy of the product. Although it is less comprehensive than professional labeling, patient labeling is intended to provide patients prescribed the medication with information that will help them use their medication effectively and safely. It should also, therefore, provide potential users with appropriately written product information they may want to consider.

FDA believes that such FDA-approved patient labeling generally meets the brief summary requirements, and, because it is written for patients, is a more appropriate vehicle for communicating risk information to consumers than the technically-written brief summary. FDA is requesting comment on its intention to consider the reprinting of certain FDA-approved patient labeling as adequate to fulfill the brief summary requirement in consumer-directed advertisements for prescription drug and biological products. The following products offer prototypical examples of such comprehensive patient labeling: Oral contraceptives, estrogenic products, Cardura®, Fosamax®, Glucophage®, Hytrin®, Proscar®, Seldane®, and Ticlid®.

Not all FDA-approved patient labeling, however, generally meets the brief summary requirements. Some approved patient labeling primarily is intended to give instructions for use (e.g., directions on how to use medications delivered via inhalation, nasal spray, patch, or injection). Other patient labeling focuses primarily on a single warning (e.g., Accutane® , the class auxiliary warning labels on angiotensin-converting-enzyme (ACE) inhibitors and isoproterenol inhalers). In both of these instances, the patient labeling has a narrow focus that is not intended to offer comprehensive risk information to patients. Because of this narrow focus, such patient labeling would not generally meet the brief summary requirements and would not be considered acceptable consumer brief summaries.

FDA also notes that many manufacturers have voluntarily produced informational brochures and other product-specific materials for patients that are disseminated through various outlets. These materials are typically submitted to the agency either for prior review and comment, or through the postmarketing review process specified in 21 CFR 314.81(b)(3)(i). Such materials that have not been through the formal labeling review process should not be considered automatically acceptable as a consumer brief summary. Instead, they may be used as brief summaries only if they fulfill all of the applicable requirements in § 202.1(e).

IV. Requests for Comments on Other Issues

Many complex public health issues are raised by DTC promotion. In the August 16, 1995, Federal Register document, FDA solicited broad public comment on the major issues concerning DTC promotion and whether the agency's current regulatory approach should be modified. Some of these issues were specifically addressed in testimony and written comments. These raised additional questions, about which FDA is now soliciting public comment.

1. Currently, § 202.1(e) states that the brief summary shall include information relating to side effects, warnings, precautions, contraindications, and other risk information. In print advertising, this requirement is generally fulfilled by including the risk-related sections of the approved labeling in, or adjacent to, the advertisement. For advertisements broadcast through media such as radio, television, and telephone communications systems, § 202.1(e)(1) provides that the advertisement ''shall include information relating to the major side effects and contraindications of the advertised drugs in the audio or audio and visual parts of the presentation and unless adequate provision is made for dissemination of the approved or permitted package labeling in connection with the broadcast presentation shall contain a brief summary of all necessary information related to side effects and contraindications.''

In addition, section 502(r) of the act requires that advertisements for restricted devices contain a brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and contraindications.

Much testimony, petitions, and comments questioned the usefulness, for consumers, of the existing ''brief summary'' of risk information that results from application of these requirements. Many comments contended that, for consumer advertising, a shorter, more focused presentation of user-friendly information could meet the statutory requirement and also provide appropriate risk-related information. Some comments suggested that a consumer brief summary should include ''information relating to the major side effects and contraindications'' of the product, as currently required in prescription drug and biological product

[1] This does not apply to submissions required in a premarket notification submission or premarket approval application (PMA) under 21 CFR 807.87(e) and 814.20(b)(10) or submissions required in connection with accelerated approval under 21 CFR 314.550 and 601.45.

broadcast advertising. (This information has colloquially been referred to as the ''major statement.'')

If FDA required or permitted more limited risk information in place of the current brief summary, what specific information should be included? What criteria should be used by manufacturers and the agency to identify the ''major'' risk information for any particular product? FDA is also interested in empirical research that specifically addresses the issues of how much and what kind of risk information can and should be communicated in DTC advertising of prescription drug and biological products.

2. Some comments suggested that risk information could be communicated to consumers through standardized general disclosures. This kind of disclosure would not reference particular characteristics of a product. Instead, such statements would reference one or more general risks, such as the fact that all prescription drug and biological products have side effects; that they are only available from a physician or other prescribing health care professional; that they have significant benefits, but may have significant risks; that patients should discuss product risks with a physician, etc.

Such disclosures, however, are susceptible to habituation or ''wear-out,'' which results in the viewer quickly learning to ignore the message, thus lowering its effectiveness. In addition, such messages may not be perceived as risk messages at all, but instead interpreted as reassurances. If the latter is the case, these messages would not fulfill the purpose of the brief summary requirement, which helps ensure that advertising conveys a balanced impression about the product's benefits and risks.

FDA solicits comments on the effectiveness of such standardized general disclosures at transmitting risk information. FDA is especially interested in any research that addresses the issue of the effectiveness of general risk disclosures of the type described above.

3. Promotional materials appear in very different media that each have distinctive characteristics (e.g., print, broadcast, telephone communications, facsimile, Internet). Should FDA require or permit different disclosures for consumer-directed promotion of prescription drug and biological products that appears in different media, to reflect the capabilities of these varying media, or should the disclosure be the same regardless of medium? For example, should print media contain longer and more complete information than broadcast media because such information could be made readily available at minimal cost and because consumers of print media may be more willing, able, and/or desirous of obtaining more complete information?

4. Different products have different degrees of effectiveness. In some cases, a product that works for a relatively small percentage of the appropriate patient population is approved either because it is the only available therapy for a condition; because all other therapies for the condition also have only modest benefits; or because it has relatively few risks. Should FDA require the communication of the degree of product effectiveness in DTC promotion? How could this information be communicated most effectively?

5. It has been suggested that toll-free telephone numbers are one way that product sponsors could make required information available to audiences. FDA requests comments and information from consumers, health professionals, product sponsors and other interested individuals regarding: (a) How useful toll-free numbers are as a mechanism for obtaining or disseminating information about medical products, and (b) the costs to a sponsor of using toll-free numbers as a means of disseminating information.

FDA welcomes comments on all of the issues described above and especially invites the submission of relevant empirical research.

Dated: May 8, 1996.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 96–12022 Filed 5–13–96; 8:45 am]

BILLING CODE 4160–01–F

[Docket No. 96E–0043]

Determination of Regulatory Review Period for Purposes of Patent Extension; EPIVIR™

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined the regulatory review period for EPIVIR™ and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of an application of the Commissioner of Patents and Trademarks, Department of Commerce, for the extension of a patent which claims that human drug product.

ADDRESSES: Written comments and petitions should be directed to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Brian J. Malkin, Office of Health Affairs (HFY–20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–1382.

SUPPLEMENTARY INFORMATION: The Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98–417) and the Generic Animal Drug and Patent Term Restoration Act (Pub. L. 100–670) generally provide that a patent may be extended for a period of up to 5 years so long as the patented item (human drug product, animal drug product, medical device, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under these acts, a product's regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period consists of two periods of time: A testing phase and an approval phase. For human drug products, the testing phase begins when the exemption to permit the clinical investigations of the drug becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human drug product and continues until FDA grants permission to market the drug product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Commissioner of Patents and Trademarks may award (for example, half the testing phase must be subtracted as well as any time that may have occurred before the patent was issued), FDA's determination of the length of a regulatory review period for a human drug product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA recently approved for marketing the human drug product EPIVIR™ (lamivudine). EPIVIR™ in combination with Retrovir® (zidovudine) is indicated for the treatment of human immunodeficiency virus infection when therapy is warranted based on clinical and/or immunological evidence of disease progression. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for EPIVIR™ (U.S. Patent No. 5,047,407) from Glaxo Wellcome, Inc., and the Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated March 1, 1996, FDA advised the Patent and Trademark Office that this human