

and pharmaceutical industry trade organizations, the American Medical Association (AMA), and the CDC in conjunction with FDA.

(Response) The agency agrees that labeling alone will not be sufficient to reduce or prevent antibiotic resistance. This final rule is one of many ongoing efforts by FDA to combat antibiotic resistance. FDA has previously and will continue to organize and participate in numerous advisory committee meetings, open public meetings, and workshops with industry and academia to focus on strategies to encourage the development of new antimicrobials while preserving the usefulness of existing drug products. Past meetings have already led to changes in the collection of clinical data by stakeholders which will ultimately shorten the development time of future antimicrobial products. The agency has an ongoing partnership with other government agencies and medical organizations to educate the public about the proper use of antimicrobials and the risks of inappropriate use. FDA has recently awarded a contract to a company to obtain antimicrobial resistance surveillance information in an effort to help the agency identify resistant organisms that pose a significant health threat to the public.

(Comment 8) One comment urged FDA to focus on the effective implementation of existing guidelines, such as the CDC guidelines for the treatment of acute otitis media in children and the Sinus and Allergy Health Partnership guidelines for the treatment of acute bacterial sinusitis, as a means of addressing antibiotic resistance. The comment added that these guidelines are both comprehensive and able to be updated as new information becomes available, whereas labeling cannot be updated quickly.

(Response) Many responsible organizations issue guidelines for the treatment of various types of bacterial infections. FDA supports these efforts and has worked with many of the sponsoring organizations to develop guidelines for clinical studies and related matters. The agency disagrees that labeling cannot be updated as quickly as guidelines. Guidelines for the treatment of bacterial infections are not usually revised more often than every 2 years. If necessary, FDA's professional labeling can be revised in 2 years.

(Comment 9) Another comment stated that peer review of antimicrobial use and prescribing practices is preferred over static treatment guidelines and restrictions, given the complexity of the decisionmaking process in evaluating patients.

(Response) The labeling statements required by this final rule are not static treatment guidelines or restrictions. Furthermore, nothing in the final rule forecloses the use of peer review as a way of reducing antibiotic resistance. FDA recognizes that many different approaches can assist physicians in making good prescribing decisions.

(Comment 10) One comment asserted that resistant infections are most often acquired in hospitals and then spread to the community and, therefore, FDA should work with public health agencies and state boards of health to establish more effective hospital infection-control programs, rather than addressing the resistance problem through labeling.

(Response) FDA is working with the CDC and other public health agencies to establish more effective hospital infection-control programs and to develop means for educating physicians and communicating current information on the resistance problem. However, the agency believes that antibiotic resistance labeling is also needed as a part of a multifaceted attack on the resistance problem. FDA also notes that some resistant organisms, for example, penicillin-resistant *Streptococcus pneumoniae*, are acquired in the community, rather than in the hospital.

(Comment 11) One comment endorsed the development and implementation of a coordinated plan for monitoring antimicrobial resistance at the local level using standardized tests. This comment stated that the use of universally accepted standard tests is critical to the consistent and meaningful interpretation of surveillance data throughout the United States and that these standards need to be in place before collecting and collating surveillance data. Without such standards, collated surveillance data would be difficult to interpret and of very limited value.

(Response) FDA is working with the CDC and other agencies to develop tools and methods that will allow for a coordinated plan for monitoring antibiotic resistance. However, efforts to curb the development of antibiotic resistance should not be delayed pending the creation of such a monitoring plan.

(Comment 12) Another comment suggested requiring a special prescription blank for antimicrobials, formatted to include FDA criteria for prescribing antibiotics, and placing the responsibility on pharmacists to ensure that the criteria are met.

(Response) Such a restriction would be extraordinarily difficult to implement because of the large number of systemic

antibacterial products. The agency believes that measures less restrictive of medical practice are more reasonable at this time.

(Comment 13) One comment recommended that marketed antibiotics be evaluated and that older products with higher potential for inducing resistance (i.e., poor PKs and/or potency, single-step resistance development) be retired in favor of newer antibiotics with optimized PKs, potency, and multiple-step pathways. This comment contended that doctors need to be educated to prescribe improved antibiotics and asserted that the rule might hinder this goal.

(Response) FDA does not agree that newer antibiotics are necessarily preferable to older ones. While some newer antibiotics may require more than one pathway to develop resistance, newer antibiotics tend to be broad-spectrum, which, in itself, can increase the development of resistance.

(Comment 14) One comment stated that the antibiotic labeling proposal should be coordinated with other agency labeling initiatives.

(Response) Rulemaking requires an opportunity for the public to comment and thus have input into proposed agency actions. To make it easy for the public to comment on only those issues that are of interest, FDA generally pursues separate rulemakings for labeling proposals concerning different subjects. FDA has proposed to revise the content and format of labeling for prescription drugs (physician labeling rule) (65 FR 81082, December 22, 2000). The agency has received comments on the proposal and is in the process of finalizing it. Whether the requirements of the physician labeling rule will apply to a systemic antibacterial drug product will depend on the approval date of that product. For those systemic antibacterial drug products that must comply with the physician labeling rule by using the new format, the final physician labeling rule will explain where in the new format the statements required by § 201.24 should be placed and when implementation of the new format must be completed.

#### E. Scope and Implementation

(Comment 15) A number of comments addressed the scope of the proposal. One comment stated that resistance can also develop from using topical, veterinary, and antimycobacterial antibiotics, and that there should be education about all these sources. One comment stated that the proposed rule should also apply to prescription and over-the-counter (OTC) otic, ophthalmic, and topical agents. One