

the specific consequences of failure to take antibiotics as directed.

(Comment 39) One comment asserted that, as written, the statement could suggest that patients are qualified and capable of diagnosing their own infections. Another comment stated that patient information should primarily reinforce the prescribed dosing because patients should not be expected to know how to distinguish between viral and bacterial infections. The comment also asserted that patients should be educated that at least one office visit is necessary to decide whether an antibiotic should be prescribed. Another comment stated that pharmacists should give patients the entire package insert rather than a summary, because patient demand for antibiotics often leads to unnecessary prescribing.

(Response) FDA does not agree that its proposed language suggests that patients are capable of diagnosing their own infections or are able to tell the difference between a viral and a bacterial infection. Generally, FDA expects that information concerning the use of antibiotics would be communicated to the patient in the doctor's office after the patient had already decided to seek medical care. However, because antibiotics are prescribed in hospitals as well as on an outpatient basis, FDA declines to adopt the suggestion that patients be told that at least one office visit is necessary. It is not clear how giving the package insert to patients who are prescribed antibiotics would reduce patient demand for antibiotics. In any event, FDA usually requires patient package inserts only when there is a need to communicate detailed risk information about a drug product or instructions for using the product. Neither of these circumstances apply to systemic antibacterial drug products.

(Comment 40) One comment stated that the patient information statement should not apply to any antibiotic administered solely via intravenous or intramuscular routes because patients do not self-administer by these routes.

(Response) FDA disagrees with the notion that patients never self-administer antibiotics by intravenous or intramuscular routes. Patients who are started on intravenous antibiotics in the hospital sometimes continue to use injectable antibiotics on an outpatient basis. Therefore, the patient information section must be included in the labeling of systemic antibacterials administered intravenously or intramuscularly.

(Comment 41) The agency received many specific suggestions for revisions to the proposed patient statement. One comment proposed the following

language: "Patients should be counseled about the differences between viral and bacterial infections." One comment suggested adding the phrase "the oral antibiotic" before the name of the product in the first sentence. Another suggestion was to add the words "despite feeling better or 'totally' well" after the phrase "Skipping doses and not completing the full course of therapy." Another comment suggested using the phrase "likelihood of selecting bacteria" rather than the phrase "likelihood that bacterial will develop."

Two comments suggested adding either "antibacterial drugs, including" or "antibacterial agents including" before the product name in the first sentence. One comment suggested replacing the specific product name in the last sentence with the phrase "antibacterial drugs," while another comment proposed to add "or other antibacterials" after the product name in the last sentence. In the sentence "Skipping doses and not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop that will not be treatable by (*insert name of antibacterial drug product*) in the future," one comment proposed to replace the first "will" with "may," while another comment suggested replacing both instances of the word "will" with the word "may."

(Response) In the final rule, FDA has adopted a number of the suggestions made in the comments. FDA has adopted the suggestion to precede the name of the product in the first sentence with the phrase "antibacterial drugs including" because the information applies to all antibacterial drugs. The agency also agrees with the idea of adding the phrase "or other antibacterials" to the last sentence, but has altered the wording slightly to state "or other antibacterial drugs." FDA agrees with the concept that patients should be told to continue therapy even after they feel better and has included the phrase "Patients should be told that although it is common to feel better early in the course of therapy * * *" in the statement.

FDA declines to adopt other suggestions. The agency believes that the suggestion that patients be counseled about the differences between bacterial and viral infections is not as direct as and, therefore, not preferable to FDA's revised language. FDA does not agree that the phrase "the oral antibiotic" should be added because the implication of this suggestion is that patients are never responsible for using injectable antibiotics. As discussed

previously, there are circumstances where injectable antibiotics are self-administered. The agency rejects the suggestion to use the phrase "likelihood of selecting bacteria" because most lay people are not familiar with the concept of bacterial selection. The agency declines to adopt the suggestions to use "may" rather than "will" in the phrases "will develop" and "will not be treatable." The concept of possibility rather than certainty is already expressed by the words "may" and "likelihood" earlier in the sentence.

IV. Environmental Impact

The agency has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

V. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule has a significant economic impact on a substantial number of small entities, an agency must consider alternatives that would minimize the economic impact of the rule on small entities. Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million in any one year (adjusted annually for inflation).

The agency believes that the final rule is consistent with the regulatory philosophy and principles identified in Executive Order 12866 and in these two statutes. The final rule will amend the content of the professional labeling for human prescription antibacterial drugs. Based on the analysis, summarized in table 1 of this document, FDA projects the annualized costs to comply with the final rule to be less than \$600,000. The agency finds that if the revised labeling reduces direct and indirect costs attributable to resistant bacteria by 1