

increase resistance if patients do not comply with the full course of therapy or otherwise alter the prescribed dosing regimen.

(Response) In response to the comments, the agency has decided not to use the words “appropriate” or “inappropriate” because it recognizes that determining appropriate use, and therefore what is not appropriate, involves many factors and requires the exercise of the physician’s judgment in using available information to select an antibiotic for a particular patient in a particular context. Instead, FDA has revised the statement under the product name to directly link reducing antibiotic resistance with prescribing antibiotics only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria. Similarly, the statement in the “Precautions” section indicates that prescribing antibiotics in the absence of a proven or strongly suspected bacterial infection increases the risk of developing resistance.

(Comment 26) One comment offered the following examples of inappropriate use: (1) Using antibiotics for common respiratory viral infections, (2) using a broad-spectrum antibiotic when a narrower spectrum antibiotic would be more appropriate, (3) using an antibiotic with an excessively long half-life, and (4) using a less potent antibiotic when a more potent agent would be more appropriate. Another comment described inappropriate use as including the use of antibiotics to treat viral infections, failure to prescribe an adequate length of treatment, failure of patients to complete the entire course of treatment, and skipping doses. This comment stated that it is important for physicians and the public to understand the basic value of antibiotics and went on to say that only inappropriate usage should be highlighted as requiring further education and restraint.

(Response) As discussed in the response to comment 25, the agency has decided not to use the words “appropriate” or “inappropriate” in the labeling statements required by this rule. The agency agrees, however, that examples of inappropriate use may include using antibiotics for viral infections, failure to prescribe an adequate length of treatment, failure of patients to complete the entire course of treatment, skipping doses, and using a broad-spectrum antibiotic when a narrower spectrum antibiotic would be more appropriate. The agency does not agree that it is never appropriate to use an antibiotic with a very long half-life. Half-life is a factor to be considered along with other many other specific factors involved in patient management,

but it is not appropriate to make generalizations about it in the context of this rule. Furthermore, focusing on the potency of an antibiotic is not a helpful approach because there is no standard definition of the potency of an antibiotic.

(Comment 27) The agency received the following five suggestions for wording to appear in place of that proposed to appear under the product name. Suggestions 1 through 4 were also proposed for the “Precautions” section:

1. “Inappropriate use of antibiotic products may increase the prevalence of drug resistant microorganisms, leading to a potential decrease in the general overall effectiveness of antimicrobial agents.”

2. “Appropriate use of antimicrobial agents may help decrease the prevalence of drug resistant microorganisms, resulting in the continued effectiveness of this product and related agents. This product should be used only to treat infections that are strongly suspected or proven to be caused by susceptible microorganisms.”

3. “Inappropriate use of an antibiotic may increase the prevalence of drug-resistant microorganisms and may decrease the future effectiveness of the antibiotic and related antimicrobial agents. It is not appropriate to extrapolate the benefit/risk profile established in patients with documented bacterial infections to other patients (e.g., patients with viral infections). This antibiotic does not treat viral infections.”

4. “Appropriate antibiotic use requires the selection of an antibiotic, for a known or suspected bacterial infection, that optimizes clinical therapeutic effect by maximizing bacteriological eradication and minimizing the development of resistance and drug-related toxicity. In order to eradicate the bacteria and minimize the development of bacterial resistance, it is important to administer the appropriate antibiotic at the right dose and for the right duration. See Dosage and Administration Section.”

5. “Inappropriate use of antibacterial agents, including (insert name of antibacterial drug product) may increase the prevalence of drug resistant bacteria and may decrease the effectiveness of antibacterial agents, including (insert name of antibacterial drug product). (Insert name of antibacterial drug product) should be used only to treat infections that are proven or suspected to be caused by indicated bacteria.”

Suggestion 5 eliminates from the proposed phrase “strongly suspected” the word “strongly,” contending that it adds nothing.

The agency also received a suggestion intended only for the “Precautions” section:

“Inappropriate use of antibacterial agents, including (insert name of antibacterial drug product) may increase the prevalence of drug resistant bacteria and may decrease the effectiveness of antibacterial agents, including the drug product. Antibacterial agents, including the drug product, should be used to treat infections that are proven or suspected to be caused by indicated bacteria. The antibacterial agent chosen to treat a documented or presumptive bacterial infection should be targeted to the most likely bacterial pathogen(s) and should have the narrowest spectrum possible to cover the likely pathogen(s).”

(Response) All of the previous wording suggestions are phrased in terms of either inappropriate or appropriate use. The agency has been persuaded by the comments that using the words “inappropriate” or “appropriate” is confusing and unhelpful; therefore, the final rule does not use these terms. Because FDA has decided not to use the words “inappropriate” or “appropriate,” the agency declines to adopt any of the wordings suggested in the comments. The agency disagrees with the opinion that there is no difference between “suspected” and “strongly suspected.” Since many infections could theoretically be either viral or bacterial, the direction to use antibiotics for suspected bacterial infections could be interpreted as approving of antibiotic use whenever there is a possibility of a bacterial infection. Therefore, the final rule retains the word “strongly.”

H. Culture and Susceptibility Tests

Proposed § 201.24(b) would have required the following statement in the “Clinical Pharmacology” section: “Appropriate use of (insert name of antibacterial drug product) includes, where applicable, identification of the causative microorganism and determination of its susceptibility profile.”

(Comment 28) Many comments objected to this statement, asserting that it is not always possible or advisable to do cultures. Comments stated that for the majority of infections, including respiratory tract infections, obtaining a specimen for a culture is not possible. One comment objected that diagnostic tests that immediately distinguish viral and bacterial infections are not available.

(Response) The agency recognizes that it is not possible to obtain specimens for cultures for many common community-