January 2012

ANTIBIOTICS

FDA Needs to Do More to Ensure That Drug Labels Contain Up-to-Date Information

GAO Accountability * Integrity * Reliability

Highlights

Highlights of GAO-12-218, a report to congressional committees

Why GAO Did This Study

Antibiotics are critical drugs that have saved millions of lives. Growing bacterial resistance to existing drugs and the fact that few new drugs are in development are public health concerns. The Food and Drug Administration Amendments Act of 2007 (FDAAA) required the Food and Drug Administration (FDA), an agency within the Department of Health and Human Services (HHS), to identify, periodically update, and make publicly available up-to-date breakpoints, the concentrations at which bacteria are categorized as susceptible to an antibiotic. Breakpoints are a required part of an antibiotic's label and are used by providers to determine appropriate treatments. FDAAA provided a financial incentive for antibiotic innovation and required FDA to hold a public meeting on antibiotic incentives and innovation. FDAAA directed GAO to report on the impact of these provisions on new drugs. This report (1) assesses FDA's efforts to help preserve antibiotic effectiveness by ensuring breakpoints on labels are up to date and (2) examines the impact of the antibiotic innovation provisions. GAO examined FDA data, guidance, and other documents; interviewed FDA officials; and obtained information from drug sponsors, such as manufacturers, that market antibiotics.

What GAO Recommends

GAO recommends that the Commissioner of FDA take steps to help ensure antibiotic labels contain up-to-date information, such as by expediting the agency's review of breakpoint submissions. HHS said it will consider implementing GAO's recommendations.

View GAO-12-218. For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov.

What GAO Found

FDA has not taken sufficient steps to ensure that antibiotic labels contain up-to-date breakpoints. FDA designates certain drugs as "reference-listed drugs" and the sponsors of these drugs play an important role in ensuring the accuracy of drug labels. Reference-listed drugs are approved drug products to which generic versions are compared. As of November 2011, FDA had not yet confirmed whether the breakpoints on the majority of reference-listed antibiotics labels were up to date. FDA contacted sponsors of 210 antibiotics in early 2008 to remind sponsors of the importance of maintaining their labels and requested that they assess whether the breakpoints on their drugs' labels were up to date. Sponsors were asked to submit evidence to FDA showing that the breakpoints were either current or needed revision. As of November 2011, over 3.5 years after FDA contacted sponsors, the agency had not yet confirmed whether the breakpoints on the labels of 70 percent, or 146 of the 210 antibiotics, were up to date. FDA has not ensured that sponsors have fulfilled the responsibilities outlined in the early 2008 letters. For those submissions FDA has received, it has often taken over a year for FDA to complete its review. Officials attributed this delay to reviewers' workload, challenging scientific issues or difficulties in obtaining needed data, and incomplete submissions. FDA also issued guidance to clarify sponsors' responsibility to evaluate and maintain up-to-date breakpoints. The guidance reminded sponsors that they are required to maintain accurate labels and stated that certain sponsors should submit an evaluation of breakpoints on their antibiotic labels to FDA annually. However, FDA has not been systematically tracking whether sponsors are providing these annual updates. Some sponsors remain confused about their responsibility to evaluate and maintain up-to-date breakpoints. At GAO's request, FDA reviewed a small sample of annual reports and determined that few sponsors appear to be responsive to the guidance.

The FDAAA provisions related to antibiotic innovation have not resulted in the submission of new drug applications for antibiotics. FDAAA extended the period of time that sponsors of new drugs that meet certain criteria have exclusive right to market the drug. According to FDA officials, the agency has received very few inquiries regarding this provision and, as of November 2011, no new drug applications for antibiotics have been submitted that would qualify for this exclusivity. None of the drug sponsors GAO received comments from said that this provision provided sufficient incentive to develop a new antibiotic of this type. FDAAA also required that FDA hold a public meeting to discuss whether and how existing or potential incentives could be applied to promote the development of antibiotics. Both financial and regulatory incentives were discussed at FDA's 2008 meeting, including tax incentives for research and development and providing greater regulatory clarity during the drug approval process.