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RESEARCH NOTES

United States Food and Drug Administration Advisory Committee outcomes and agency approval analysis from 2010 to 2015

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ABSTRACT

Objectives: This analysis sought to quantify voting behavior and other characteristics of advisory committee (AC) meetings and compare that with the U.S. Food and Drug Administration's (FDA) approval decisions from 2010 to 2015.

Methods: The analysis of the Center for Drug Evaluation and Research AC meetings was conducted using publicly available information from the FDA website and the sponsors' websites.

Results: There were 163 voting sessions, 207 votes, and 229 meetings. Voting questions assessed approval (63%), acceptable risk-benefit profile (19%), efficacy (8%), safety and efficacy (7%), and safety (3%). The AC voted in favor of approval 67% of the time and against approval 33% of the time, although it heavily favored one outcome when voting favorably or unfavorably. The FDA approval decision supported the committee's decision in 90% of cases. When such agreement did not occur, it was due to differences in clinical opinion (43%), manufacturing deficiencies (14%), lack of manufacturing data (14%), and a post-AC event (5%). There was insufficient information to determine why there was a differing opinion in 24% of cases. When FDA had a differing opinion, the agency typically did not approve a substance in which the committee recommended approval (81%).

Conclusion: The results support past research examining the topic from 2001 to 2010. Voting patterns were relatively constant, and they generally heavily favored one outcome. The FDA's ultimate approval decision was in line with the AC vote the vast majority of cases. Any disagreement was usually due to FDA having a differing opinion regarding clinical importance, furthering the notion that AC insight is heavily considered but not the final determinant in agency action. This topic has importance in understanding pharmaceutical approval in the United States, and this has clinical practice implications.

Advisory committee (AC) meetings hosted by the United States Food and Drug Administration (FDA) are part of the premarket approval process for many pharmaceuticals in which the opinions of external experts are solicited to help address areas of uncertainty. Generally, ACs are composed of a chair, members, and occasionally a consumer, industry, and patient representative. These experts offer their independent advice on a variety of topics, including issues related to human drugs.[1] AC meetings are of substantial importance to pharmaceutical manufacturers, also known as *sponsors*, because they are convened after meaningful time and financial investment and can have a large influence in a drug's ultimate approval. FDA is not required to follow the AC recommendation; however, given the experience and knowledge of the independent experts, recommendations made by ACs are taken seriously by FDA. As a result, an analysis has been performed to quantify voting behavior and other characteristics of AC meetings and to compare that with the FDA's approval decisions. The McKinsey Center for Government released an FDA Advisory Committee Outcomes assessment in which different characteristics of Center for Drug Evaluation and Research (CDER) AC meetings between 2001 and 2010 were quantified.[2] In particular, a subset of 63 of the 281 AC meetings focused on approval for a new drug or biologic during this 10-year period examined the extent FDA agreed with the ACs

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recommendation. It was found that FDA approved 88% of the products endorsed by the ACs and did not approve 86% of those that the ACs did not endorse.

Current literature

The McKinsey Center for Government, which is a portion of McKinsey & Company, is a center for research aiming to improve performance and productivity in government.[3] This group conducted an assessment to quantify AC characteristics during 2001-2010, which included quantifying the number of meetings in which there was a vote on approving a product and identifying which ACs had the most meetings to vote on approval questions. In addition, the assessment identified the percentage of approved new molecular entities that were the subject of an AC meeting and, for a subsect of meetings, the extent to which FDA followed an AC recommendation on whether a product should be approved. To our knowledge, this is the only publicly available analysis identified by the author.

Objective

Although the McKinsey review is insightful, it is not comprehensive of all ACs and is no longer current given it reviews information up to 2010. To maintain an understanding of the influence ACs have in a frequently evolving regulatory landscape, an analysis was performed across all CDER ACs during 2010-2015 in an attempt to assess the extent that the FDA's pharmaceutical approval decision followed the AC recommendation and, when it did not, the reason for the dissent. This review examined all approval-related decisions of the ACs during this window.

Methods

An analysis of CDER AC meetings during 2010-2015 was conducted using publicly available information. Information pertaining to the AC (number of voting sessions, votes, and meetings; percent of meetings that were joint meetings; percent of committee members voting yes, no, abstain, or nonvoting; and breakdown of voting question) was obtained from the FDA website, particularly from available meeting minutes and transcripts for each AC.[4] Information regarding the FDA decision regarding approval and its rationale for issuing a complete response letter was based on material gathered from the FDA website[5] or directly from the sponsor's website. In some circumstances, it was not possible to identify the reason behind a pharmaceutical receiving a complete response letter, as the sponsor chose to keep this information confidential. Microsoft Excel was used to aggregate and assess the compiled data.

In conducting the assessment, a distinction was made between "advisory committee meetings," "voting sessions," and "votes." *AC meetings* refers to the act of hosting a meeting (e.g., on March 9, 2015, the Dermatologic and Ophthalmic Drugs AC held a meeting). AC meetings can be held by one committee or can be joint meetings if held in conjunction with another committee (e.g., on May 2, 2011, the Cardiovascular and Renal Drugs AC and Drug Safety and Risk Management AC held a joint meeting). Joint meetings were counted only once when totaling the number of meetings during 2010-2015. AC meetings were further subdivided into "voting sessions" and "votes." AC meetings either explored 1 topic throughout the day (1 voting session) or had 2 distinct sessions in the morning and afternoon (2 voting sessions). During these voting sessions, each question for which a vote was taken was counted as a vote.

For questions in which a vote took place, the voting behavior of an advisory committee panelist was classified as "yes," "no," "abstain," or "nonvoting." This was done to maintain consistency with the format provided by FDA in online meeting minutes. A "yes" vote meant that the panelist voted in favor of the question. A "no" vote meant that the panelist voted not in favor of the question. An "abstain" vote meant that the panelist did not vote "yes" or "no," typically because of the belief that there was insufficient information to answer the question. *Nonvoting* meant that a panelist did not vote, which could be due to having to leave the AC before the vote was held.

Table 1
FDA advisory committees

2010	2011	2012	2013	2014	2015
Anesthetic and life support drugs		Anesthetic and analgesic drug products			
Anti-infective drugs					Antimicrobial drugs
Antiviral drugs				N/A	
Arthritis					
Reproductive health drugs				Bone, reproductive, and urologic drugs	
Cardiovascular and renal drugs					
Dermatologic and ophthalmic drugs					
Drug safety and risk management					
Endocrinologic and metabolic drugs					
Gastrointestinal drugs					
N/A			Medical imaging drugs	N/A	
Nonprescription drugs					
Oncologic drugs					
Peripheral and central nervous system drugs					
Pharmaceutical science and clinical pharmacology				N/A	
N/A					Pharmacy compounding
Psychopharmacologic drugs					
Pulmonary-allergy drugs					