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Califf And Advisory Committees: Will He Push For Reforms?

by Derrick Gingery

Confirmation hearing comment suggests FDA Commissioner nominee Robert Califf thinks an overwhelming advisory committee vote should give agency officials pause.

Robert Califf may be willing to give advisory committee opinions a little more influence should he become commissioner of the US Food and Drug Administration.

Califf hinted during his 14 December Senate confirmation hearing that an overwhelming advisory committee vote should warrant close scrutiny by agency officials before making a decision.

“I think when there’s an 11-2 vote the leaders at FDA really need to take a close look and make sure they’ve got it right,” he said before being interrupted.

His comment about taking a close look could suggest that he believes the opinions of outside advisors should carry more weight, especially in light of recent complaints about the agency’s use of its advisory committees and calls for reform. Califf could influence any changes should he be confirmed.

After the FDA granted an accelerated approval for *Biogen, Inc.*/*Eisai Co., Ltd.*’s Alzheimer’s treatment Aduhelm (aducanumab-avwa) despite a largely negative advisory committee vote, several members resigned from the body in protest. (Also see "*Aduhelm Approval Firestorm Raises Question: What Are US FDA Advisory Committees For, Anyway?*" - Pink Sheet, 11 Jun, 2021.)

The backlash lead the Center for Drug Evaluation and Research to launch an advisory committee meeting reform effort. CDER Director Patrizia Cavazzoni wants to refocus the sessions on science rather than emotion. (Also see "*US FDA Advisory Committees Could Get Revamp With A Focus On Science Over Emotion*" - Pink Sheet, 15 Jun, 2021.) The FDA also is considering policy on

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when advisory committee meetings are appropriate. (Also see "*US FDA Adcomm Modernization Includes How Meetings Are Scheduled*" - Pink Sheet, 17 Aug, 2021.)

A survey of advisory committee members also found that many felt the FDA should not approve a product when the number of negative votes reaches a certain threshold. (Also see "*Power To The (Adcomm) People: Members Believe Votes Should More Directly Affect US FDA Decisions*" - Pink Sheet, 17 Aug, 2021.)

The advisory committee issue emerged in an opioids context, but Califf broadened his response to include all decisions. Sen. Ben Ray Luján, D-NM, asked Califf for his reaction to the 11-2 advisory committee vote against approval of *Zogenix, Inc.*'s Zohydro ER (hydrocodone) in 2012. Luján wanted Califf to admit the approval was a mistake.

The agency approved the product despite the vote. Califf said that if long-term studies had been completed at the time of the review, the decision would have been different. During his first term as commissioner, Califf said the committee should have met again to consider postmarketing plan changes the FDA proposed. (Also see "*Robert Califf Likely To Find Many Familiar Problems Upon His Return To US FDA*" - Pink Sheet, 12 Nov, 2021.)

Califf also said that FDA staff only disagree with advisory committee decisions about 25% of the time and in three-quarters of those cases it is for a more restrictive product use.

Former FDA Officials Accuse FDA Of 'Sidelining' Vaccine Advisory Committee

Two days after the confirmation hearing, two former FDA officials criticized the agency for refusing to engage its advisory committee to discuss COVID-19 vaccine boosters.

In a *Washington Post Op-Ed* headlined "The Biden Administration has been Sidelining Vaccines Experts," Philip Krause, a former deputy director of the FDA Office of Vaccines Research and Review, and Luciana Borio, a former agency chief scientist, argued the FDA should have solicited an advisory committee opinion before authorizing booster shots for all adults, as well as those age 16 and 17.

Krause and Borio said the lack of public discussion meant that "the costs and benefits of these policy moves, from a

COVID Vaccine Authorization Changes Without Advisory Committee Becoming More Common

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Decision to allow boosters for 12- to 15-year-old recipients of the Pfizer/BioNTech vaccine will go before CDC's ACIP, but like several other recent changes for COVID vaccines, the US FDA opted to skip its advisory committee.

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medical perspective, were not fully aired publicly and discussed in advance."

Read the full article here

"At this point in the pandemic, the world faces a host of new questions related to vaccines and boosting," they wrote. "The recommendations of experts on the outside advisory committees are needed more than ever so the scientific community can understand the empirical bases for decisions, and so the public can be assured that science, not politics, is driving vaccine policy."

In making the decision on booster shots, the FDA argued that advisory committee members had previously discussed the issue and that the requests did not merit another session. (Also see "*Same Data, Broader Use: COVID-19 mRNA Vaccine Booster Authorizations Expanded In US*" - Pink Sheet, 19 Nov, 2021.)

Borio and Krause wrote that reasoning was unpersuasive, given the previous views of the panel.

"Exigency might be offered as an excuse for bypassing the advisory process, but that's the exact circumstance when expert discussion and interpretation of the data can make the biggest difference," they said.

Since then, FDA has expanded the authorization for boosters to those 12 and up, also without convening an advisory committee. (*See sidebar.*)

FDA officials also did not convene the Vaccines and Related Biological Products Advisory Committee before updating COVID-19 vaccine safety information to include that the risk of myocarditis and pericarditis was higher with the *Moderna, Inc.* product compared to the *Pfizer Inc.*/*BioNTech SE* vaccine. (Also see "*US FDA Tags Moderna COVID-19 Vaccine With Higher Myocarditis Risk Than Pfizer/BioNTech*" - Pink Sheet, 1 Dec, 2021.)

In addition, the agency did not seek advisory committee input on updating the *Janssen Biotech Inc.* vaccine fact sheet to include the increased risk of thrombosis with thrombocytopenia syndrome (TTS). That change lead the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices to recommend preference for the Pfizer/BioNTech and Moderna vaccines over the Janssen product. (Also see "*ACIP Prefers mRNA COVID-19 Vaccines, But Worries Message May Not Resonate*" - Pink Sheet, 16 Dec, 2021.)