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The US FDA's Advisory Committee Drought

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FDA's external advisory committee process is under increasing scrutiny within the agency and by the public – and the agency is continuing to be very sparing in convening actual reviews.

Where are all the advisory committees?

For the first half of 2021, the US Food & Drug Administration convened just seven committees to review pending new drug applications, a pace that lags behind the already low tally of 18 product reviews in 2020. Thus far in the second half of the year, FDA has had just a single application-focused meeting, for *AstraZeneca PLC*/*FibroGen, Inc.*'s troubled roxadustat application on 15 July. (Also see "*Roxadustat Rejection Has Lessons For Other Sponsors*" - Pink Sheet, 22 Jul, 2021.)

FDA so far has no meetings on its calendar for August. The only biopharma focused committee meeting on FDA's agenda next month is a two-day review of gene therapy safety issues in clinical trials set for 2-3 September. (Also see "*Gene Therapy AAV Vector Toxicities Get US FDA's Attention*" - Pink Sheet, 26 Jul, 2021.)

The next "yes or no" event for a pending application isn't until 7 October, when *Takeda Pharmaceutical Co. Ltd.*'s maribavir goes before the Antimicrobial Drugs Advisory Committee. (Also see "*Recent And Upcoming FDA Advisory Committee Meetings*" - Pink Sheet, 30 Jul, 2021.)

There are a handful of other sponsors with pending applications who have disclosed that a meeting is expected as part of the review. They include *Eli Lilly and Company*/*Innovent Biologics, Inc.* for the non-small cell lung cancer agent, sintilimab; *Reata Pharmaceuticals, Inc.* for the Alport Syndrome/kidney disease rare disease drug, bardoxolone; and *Merck & Co., Inc.*for gefapixant, to be used in refractory chronic cough.

As in recent years, the rarity of panel stops is heightened by the breakneck pace of new drug approvals in the background. FDA appears to be on pace to set yet another all-time approval record. (Also see "*US FDA's Novel Approval Count Hits 32 In First Half Of 2021, With More Than 40*

Goal Dates Ahead" - Pink Sheet, 5 Jul, 2021.)

One recent NME approval – *Biogen, Inc.*/*Eisai Co., Ltd.*'s Alzheimer's therapy Aduhelm (aducanumab-avwa) – is also at the center of the new round of scrutiny of FDA's use of the advisory committee process.

Aduhelm was on track to be a milestone approval in 2020, under expedited review as a potential first in class disease modifying agent. However, FDA's Peripheral & CNS Drugs Advisory Committee balked at the idea of approving the drug based on a data package that included one failed trial and second that was discontinued for futility before being deemed successful.

FDA's decision to grant the application an Accelerated Approval (following extensive internal deliberations that extended the review past the original deadline and probably about six months past the originally expected approval date) stands out as one of the most high-profile and extreme cases of a decision that contradicts an outside panel vote.

That high-visibility decision both complicates and energizes an ongoing effort by FDA to review the advisory committee process, one that began independently of the Aduhelm issue but now is certain to be colored by it. (Also see "*US FDA Advisory Committees Could Get Revamp With A Focus On Science Over Emotion*" - Pink Sheet, 15 Jun, 2021.)

Critics of the agency see the Aduhelm decision as calling into question the entire purpose of the advisory committee process, and three members of the PCNS panel have resigned their spots on that committee (only two of whom actually participated in the Aduhelm review). (Also see "*Aduhelm Approval Firestorm Raises Question: What Are US FDA Advisory Committees For, Anyway?*" - Pink Sheet, 11 Jun, 2021.)

FDA, however, may have taken different lessons from the experience, given the unusually hostile tone of the meeting where members seemed to be questioning the integrity of FDA Office of Neuroscience Director Billy Dunn – apparently misinterpreting his presentation of the consensus view of the clinical team (but one that clearly disagreed with the statistical review) as some form of pushing the sponsors' point of view over the agency's. (Also see "*FDA's Mismanaged Aduhelm Review: What Went Wrong*" - Pink Sheet, 6 Jul, 2021.)

The resignations that followed the approval are likely to heighten the perception within the agency drug review leadership that committee members are susceptible to mis-reading a difference of opinion over data interpretation as a lack of integrity in the process.

The relative dearth of advisory committee meetings since the Aduhelm review may only be a coincidence – the trend in recent years has been for FDA to be every more selective in convening panels to discuss pending applications.

But it certainly underscores the long-standing conflict between the statutory directive included in the FDA Amendments Act – which frames advisory committees as the default expectation for new molecular entities – and the recent reality where FDA skips the committee is the vast majority of cases. (Also see "*US FDA's Breakneck Approval Pace Clashes With Advisory Committee Mandate*" - Pink Sheet, 9 Jan, 2020.)