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30 May 2022 | **News**

US FDA Accelerated Approval Council Required Under Senate User Fee Bill

by Sue Sutter

Intra-agency group would be tasked with ensuring consistent use of the expedited pathway across the FDA, with duties potentially including development of best practices, product review team training, and advising on withdrawals, according to the Senate's bipartisan user fee legislation.

The US FDA would be required to set up an internal council to ensure consistent application of the accelerated approval pathway under bipartisan user fee legislation introduced in the Senate on 27 May.

The Food and Drug Administration Safety and Landmark Advancements Act (*FDASLA*), introduced by Health, Education, Labor and Pensions committee chair Patty Murray, D-WA, and ranking member Richard Burr, R-NC, would require establishment of an intra-agency coordinating council "to ensure the consistent and appropriate use of accelerated approval" across the FDA.

The inclusion of provisions on accelerated approval marks a change from a draft version of the Senate bill released on 17 May, which did not address the expedited regulatory pathway. (Also see "*Accelerated Approval, Clinical Trial Diversity Provisions Left Out Of Senate User Fee Bill*" - Pink Sheet, 17 May, 2022.) Also new to the Senate measure is a provision that would require the FDA to make therapeutic equivalence evaluations for drugs approved under the 505(b)(2) pathway. *(See sidebar for story.)*

Intra-Agency Group

While many of the Senate bill's provisions on accelerated approval resemble those in the House user fee reauthorization legislation that passed out of the Energy and Commerce Committee on 18 May, the requirement for an intra-agency coordinating council is new. (Also see "*US FDA Could Require Pediatric Cancer Drug Combo Studies Under Amended User Fee Bill*" - Pink Sheet, 18 May, 2022.)

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The council would consist of at least 10 senior officials, or their designees, from various FDA units that deal with drugs and biologics. *(See box.)*

The council would be required to meet at least three times per calendar year to discuss issues related to accelerated approval, including any relevant cross-disciplinary approaches for product review.

The council's policy development activities may include:

- Developing guidance for FDA staff and best practices for, and across, product review teams, including with regard to communications between the agency and sponsors and the review of products under accelerated approval;
- Providing training for product review teams; and
- Advising review divisions on product-specific development, review and withdrawal of products under accelerated approval.

Accelerated Approval Council Membership

- Center for Drug Evaluation and Research director
- Center for Biologics Evaluation and Research director
- Oncology Center of Excellence director
- Office of New Drugs director
- Office of Orphan Products Development director
- Office of Tissues and Advanced Therapies director
- Office of Medical Policy director
- At least 3 directors of review divisions overseeing products approved under accelerated approval, including at least 1 review division director in the Office of Neuroscience

The bill calls for the council to be established within 180 days of enactment. The group must issue a public report of its activities within one year of enactment and annually thereafter.

Improving Consistency

There long have been complaints that some FDA review divisions are more flexible and willing to use the accelerated approval pathway than others.

The former includes the oncology review divisions, as cancer accounts for the bulk of drugs receiving accelerated approval. For example, among the 14 novel agents granted accelerated approval by CDER in 2021, all but three were for cancer. (Also see "*Accelerated Approval Makes*

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Big Splash In 2021 Novel Agents, Despite Crackdown On 'Dangling' Cancer Claims" - Pink Sheet, 18 Jan, 2022.)

In recent years, two of the most controversial approvals under the pathway have come outside of oncology: *Sarepta Therapeutics, Inc.*'s Duchenne muscular dystrophy drug Exondys 51 (eteplirsen) in 2016, and *Biogen, Inc.*'s Alzheimer's drug Aduhelm (aducanumab-avwa) in 2021.

Both were approved in the face of internal opposition from FDA staff, and both sparked heightened scrutiny of the expedited pathway, including the long timelines that sponsors sometimes take to complete confirmatory trials. (Also see "*3,189 Days: Aduhelm Phase IV Timeline Is Long Among Alzheimer's Drugs And Other Accelerated Approvals*" - Pink Sheet, 12 Jul, 2021.)

The Oncology Center of Excellence's recent push to withdraw accelerated approval indications for which confirmatory trials have failed ("dangling") or were never completed ("delinquent") also has drawn the attention of stakeholders and demonstrated how the agency, even without new legislation, can take a tougher stance in enforcing the timely conduct of required postmarketing studies that demonstrate clinical benefit. (Also see "*'Dangling' Cancer Indications In US: New Year Brings New Withdrawals Of Accelerated Approvals*" - Pink Sheet, 18 Jan, 2022.)

Similarities To Medical Policy Council

The proposal for an accelerated approval council is reminiscent of CDER's establishment of the internal Medical Policy Council a decade ago. That group, comprising executive-level officials within the drugs center, was aimed at addressing practical and regulatory roadblocks to approval of novel therapies and ensuring that medical policy is implemented in a consistent manner throughout the center. (Also see "*Senior CDER Management Panel Could Facilitate Novel Therapy Approval*" - Pink Sheet, 11 Jan, 2012.)

The council subsequently was tasked with reviewing breakthrough therapy designation requests. (Also see "*CDER Medical Policy Council Balances "Breakthrough" Requests With Broader Issues*" - Pink Sheet, 22 May, 2013.)

In addition, the Medical Policy Council has at times weighed in on product-specific approvability questions as well as withdrawals under the accelerated approval regulations. For example, in January 2020 the council unanimously

Therapeutic Equivalence Evaluations Would Be Required For 505(b)(2) Drugs Under Senate User Fee Bill

By Brenda Sandburg

30 May 2022
The Senate HELP Committee added a therapeutic equivalence provision to the draft measure it floated two weeks ago. The bill

agreed with a review division recommendation that *Covis Pharma*'s preterm brith prevention drug Makena (hydroxyprogesterone caproate) should be withdrawn for failure to confirm clinical benefit. (Also see "*Makena Withdrawal Hearing: US FDA Drugs Center, Covis Tussle Over Panel Composition*" - Pink Sheet, 18 Oct, 2021.)

introduced in the Senate still does not include provisions on clinical trial diversity or 180-day exclusivity.

Read the full article here

House Measures Mirrored

The Senate bill's provisions on accelerated approval withdrawal procedures and postmarketing studies generally mirror those in the House bill.

Under the expedited withdrawal provisions, an advisory committee meeting would only be held if requested by the sponsor and no such committee previously had advised the agency on issues related to withdrawal of the product at issue. (Also see "*User Fee Bill's Accelerated Approval Reform Provisions Watered Down, But Could Speed Withdrawals*" - Pink Sheet, 4 May, 2022.)

The FDA shall specify the conditions for required postapproval studies no later than the time of accelerated approval, and those conditions may include enrollment targets, study protocol and milestones, including target date of study completion. Post-approval studies for accelerated approval products could be augmented or supported by real-world evidence.

If the FDA does not require postmarketing studies for an accelerated approval product, it must publish on its website the rationale why such a study is not appropriate or necessary.

A sponsor of an accelerated approval drug must submit a report on the progress of any required postmarketing study 180 days after approval and every six months thereafter until the study is completed or terminated.

The Senate bill includes requirements for the FDA to issue guidance on:

- Early-stage meeting discussions about novel surrogate or intermediate clinical endpoints;
- Use of novel trial designs for postmarketing studies;
- Expedited withdrawal procedures under accelerated approval; and
- "Considerations related to the use of surrogate or intermediate clinical endpoints that may

support the accelerated approval of an application." (This guidance element is not included in the House legislation.)

The measure also calls for establishment of a pilot program to advance development of efficacy endpoints for rare diseases.

In the PDUFA VII commitment letter negotiated with industry, the FDA agreed to establish a pilot program to support efficacy endpoint development for rare disease treatments by offering additional engagement opportunities to sponsors of development programs that meet specific criteria. (Also see "*PDUFA VII: US FDA Will Offer Additional Meetings To Boost Rare Disease Endpoint Development*" - Pink Sheet, 30 Aug, 2021.)