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FDA Rare Disease Hub Update

Great Idea: Will Take Resources + Key Staff to Make a Difference

Relevant Companies

Our Take & Next Up

The FDA Rare Disease Hub likely takes years and new dollars allocated from the PDUFA reauthorization to make a meaningful difference in orphan drug approvals. Today, the FDA held their public meeting to detail the agency's goals for the FDA Rare Disease Innovation Hub (link here). FDA is currently in "start-up" mode and is working on establishing the Hub with limited funding as they lack additional resources from Congress. Staff capacity and participation will be critical to the success of the Hub as they will be asked to engage in additional collaborative efforts with limited reimbursement. The Hub is the fulfillment of a long-time request from the rare disease communities on establishing a type of Center of Excellence for rare diseases. And we expect it will have staying power regardless of the election results.

Key Points

The Hub is co-chaired by Drs. Peter Marks (Director of CBER) and Patrizia Cavazzoni (Director of CDER). We note that Peter Marks is a big fan of this effort and Patrizia Cavazzoni is less so, but still, the effort moves forward. Looking forward, we think the Hub could be beefed up and accelerated through additional funding via the next user fee authorizations which are due September 2027. However, additional funding from Congress may be limited or come with oversight in a GOP controlled environment as Republicans have continued to criticize the agency on transparency and spending.

What is the Rare Disease Hub? Similar to the Oncology Center of Excellence (OCE), the Hub, announced in July 2024, aims to improve and accelerate rare disease therapeutic reviews through increased collaboration between the FDA divisions and stakeholders. The Hub would have three primary functions:

- Serve as a single point of connection and engagement with the rare disease community, including patient and caregiver groups, trade organizations, and scientific/academic organizations, for matters that intersect CDER and CBER.
- Enhance intercenter collaboration to address common scientific, clinical and policy issues related to rare disease product development. This would include relevant cross-disciplinary approaches related to product review and promote consistency across offices and Centers.
- Advance regulatory science with dedicated workstreams for consideration of novel endpoints, biomarker development and assays, innovative trial design, real world evidence, and statistical methods.

The increase in rare disease products under review made a traditional Center of Excellence (COE) difficult to implement. The FDA Rare Disease Innovation Hub is a "virtual Center of Excellence" for rare disease products according to Peter Marks. Dr. Marks noted that FDA staff are kept in place with no changes to reporting structures even as they engage in the Hub. He noted that a traditional COE is unlikely for rare diseases as more than half of products that are reviewed are rare disease products, making a traditional COE too large of an entity to implement.

The Hub will specifically focus on diseases with smaller populations or diseases in which the natural history is not well understood. Therapies for ultra-rare conditions (which affect fewer than 1 in 50,000), face particular challenges from limited and imperfect data to shifting FDA requirements. While informally, the FDA is willing to grant flexibility, there is no official distinction between rare and ultra rare conditions. Stakeholders like **Ultragenyx** and **EveryLife Foundation for Rare Diseases** have previously called for an ultra-rare disease pathway which allow for a distinct criteria for ultra-rare diseases. However, the agency has resisted the push to create a designation, and we do not expect to see changes anytime soon. But the Hub provides another opportunity to discuss the needs and challenges for ultra rare conditions and we could see some internal FDA champions for addressing ultra rare conditions.

Internal FDA collaboration will be a primary focus for implementation. Knowledgeable and capable staff who are willing to be involved in additional collaborative efforts beyond their current workload will be required for the success of the Hub. The Hub's short-term goals include hiring the Director of Strategic Coalitions who will serve as the Hub's center point, aligning FDA staff on cross-center collaborations, and working on regulatory consistency through coordination of best practices between CBER and CDER.

Communication and establishing regulatory consistency are key concerns. The Hub plans to hire a Director of Strategic Coalitions who will serve as a single-entry point of communication for stakeholders. This will address the difficulty of directing rare disease concerns to the right staffers. The agency noted challenges in discussing cross cutting themes about rare disease drug development that is not related to a specific NDA. A new vehicle to have these discussions is being crafted. The agency is also conducting their own portfolio reviews and plans to take stakeholder input and their own landscape analysis to determine implementation and specific priorities.

Public comments centered on the need for improving external expertise input and improving agency coordination. Several commenters highlighted the limited expertise that FDA has for certain rare conditions and the need to facilitate outside expertise involvement. Others commented on barriers of the regulatory review process including clinical trial challenges for individualized medicines, lack of biomarkers and meaningful endpoints, and clinical trial design and cost issues for rare disease medicines.

On the current rare disease R&D landscape, there were 700+ rare disease medicines in the drug development pipeline in 2023, according to PhRMA. As a reminder, rare diseases are defined as conditions that affect less than 200,000 people in the United States. Disease areas of high drug developer interest include rare cancers (including rare blood cancers), genetic diseases, and neurological disorders. Companies with significant rare disease pipeline focus include NVS, PFE, BMY, Roche, Sanofi, AZN, Takeda, Ultragenyx (RARE), and JNJ.

Ipsita Smolinski
Managing Director I Capitol Street
ipsita@capitol-street.com

202.250.3741 I www.capitol-street.com

900 19th St NW 6th Fl
Washington, D.C. 20006

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