



February 3, 2020

The Honorable Michael Braun
United States Senate
374 Russell Senate Office Building
Washington, D.C. 20510

Dear Senator Braun,

On behalf of the 25 to 30 million Americans with one of the over 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks you for the opportunity to comment on the Conditional Approval Act (S.3133).

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the over 300 organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

The Orphan Drug Act (ODA), enacted in 1983, provides hope for many that there will one day be a treatment, if not a cure. Since enactment of the ODA, there have been over 800 indications approved by the Food and Drug Administration (FDA) to treat rare diseases. Over 90 percent of the known rare diseases, however, still do not have FDA-approved treatments. Given this lack of available rare disease treatments, when patients learn that new, promising therapies are in development, it is understandable that they should want access as soon as feasibly possible.

As a result of both changes in law and regulations, FDA now has a range of authorities that enable the agency to expedite the review of medical products at the earliest scientifically possible time and simultaneously maintain its "gold standard" that ensures safety and effectiveness. For example, manufacturers can take advantage of FDA's fast track designation, breakthrough therapy designation, priority review designation, or accelerated approval pathway.¹ In the case of serious or life-threatening diseases, however, patients may seek to acquire therapies before they reach the market.

If a patient is eligible to participate in a clinical trial of a particular product, access to these new medicines can be obtained within the confines of the trial. But, in many cases, patients are ineligible for clinical trials for one reason or another. Further, even for patients who can participate in a trial, they may want to continue taking a drug following the end of a clinical trial. To address situations in which it is appropriate for a patient to access a product outside of the clinical trial, FDA permits such access under the expanded access pathway, otherwise known as

¹ For an overview of these authorities, see:

Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review. (n.d.). Retrieved from <https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review>

“compassionate use,” which offers a mechanism for accessing investigational therapies outside of clinical trials for those with serious or life-threatening conditions.

Despite the existence of expanded access, many patients have still been unable to access investigational therapies. NORD is working to find solutions, for example by encouraging FDA to use its flexibility in clinical trial structures.² However, establishing a new so-called “conditional approval” pathway in law, as set forth in S. 3133, is simply not the solution. Rather, NORD is concerned that S. 3133 will unnecessarily weaken FDA’s approval standards, expose patients to harm, and raise patients’ hopes without delivering meaningful change.

The Federal Food, Drug, and Cosmetic Act (FFDCA) and its regulatory framework emerged as a result of exposure to what one reporter referred to as a “chamber of horrors.”³ In the early 20th century, companies could, and often did, sell products with no information on the safety or efficacy of such products, endangering the lives of patients. The 1962 Kefauver-Harris amendments to the FFDCA enshrined in law for the first time the requirement that manufacturers prove not only that a medication is safe, but also effective.⁴ A critical aspect of this requirement is the notion that all drugs must first pass through three phases of clinical trials, not just one or two, to ensure safety and effectiveness for those with the condition in question.

Permitting patient access to medicines before they have been demonstrated to be both safe and effective skirts this fundamental requirement in the FFDCA. In certain highly limited and controlled circumstances, such access may be appropriate if protections are in place. For example, the access must be equitable, access should not risk ongoing research, patients should be well-informed of the risks at hand, and the benefit of taking the therapy without knowing the entirety of its safety and efficacy profile must outweigh the risks. Under expanded access, which, again, is only available to those with serious or life-threatening conditions, FDA works with the manufacturer and the patient’s physician to ensure these circumstances are met.

Under S. 3133, however, access would not be limited to only those products indicated for a serious or life-threatening condition with unmet need and these critical protections would not exist. As drafted, the bill would apply to almost any product for any condition. The bill states that, to be eligible for conditional approval, drugs must be “intended for the treatment, prevention, or medical diagnosis of a seriously debilitating disease, life-threatening disease, or a chronic condition,” the latter of which is defined in section 524(d)(3) in a way that could be interpreted as applying to nearly every condition. Additionally, the bill includes an unclear and conflicting description of how many other treatments can be on the market to treat the same condition that an eligible drug seeks to treat. In section 524B(a)(4), there is a requirement that there be “no existing meaningful treatments,” yet in section 524B(a)(6), there is a simultaneous requirement that there be “no more than 2 meaningful treatments.” As drafted, this pathway would represent a complete overhaul of the current drug review framework designed to keep patients safe.

²<https://rarediseases.org/wp-content/uploads/2019/08/NORD-2019-Comments-on-CDER-CBER-Clinical-Trial-Eligibility-Criteria-FINAL.pdf>

³ 80 Years of the Federal Food, Drug, and Cosmetic Act. (n.d.). Retrieved from <https://www.fda.gov/about-fda/virtual-exhibits-fda-history/80-years-federal-food-drug-and-cosmetic-act>

⁴ 21 U.S.C. ch.9 §301 et seq.

Further, unlike expanded access, there is nothing in this legislation to prevent companies from developing products without any intent to ultimately seek full approval, solely with the objective of profiting off of patients desperate for an intervention. Under expanded access, companies are prohibited from profiting when they provide investigational therapies. Under S. 3133, no such prohibition applies. The failure to include a profit prohibition guts any incentive that a company would otherwise have to invest in the further studies required to obtain full approval. While the bill does call for the Secretary to require additional studies, the language is vague and does not make evident how FDA will be able to sufficiently compel a manufacturer to comply.

Allowing companies to profit could enable more companies to offer access, but it could also create access inequities and enable bad actors to profit off of false hope. Insurers are unlikely to provide coverage for therapies that are conditionally approved, which would mean, under the best of circumstances, only those who are able to afford the therapy out-of-pocket would be able to access these products. Under the worst of circumstances, only those with sufficient means would be able to obtain these therapies, and they would ultimately be ineffective or, worse, unsafe.

Further exacerbating these concerns, S. 3133 would significantly limit a manufacturer's liability in the event that an unsafe or ineffective drug injures a patient. Thus, under the bill, unscrupulous manufacturers would have a legal pathway to market an unsafe and ineffective product that ultimately injures patients--all without any responsibility to compensate patients for such injuries.

Finally, although the title of S. 3133 indicates the bill is intended to establish a "conditional" approval that lapses after a period of time, the bill fails to establish a meaningful mechanism to permit FDA to require the removal of the product from the market if the approval is not renewed. It is unclear how FDA would be able to effectively remove a therapy from the market if a drug sponsor does not procure full approval. Under current law, FDA does not have mandatory drug recall authority.

NORD is deeply concerned that, contrary to the goal of providing patients with earlier access to safe and effective medicines, S. 3133, if enacted, will serve only to harm and disappoint. Manufacturers with promising products will be unlikely to use the pathway as they will remain focused on getting full approval as soon as possible through already existing pathways, while manufacturers without promising products will have a new avenue to take advantage of patients.

NORD stands ready to work with Congress and other stakeholders to develop meaningful solutions that maintain FDA's gold standard of safety and effectiveness while preserving patient access to medicines at the earliest possible time. There is currently promising work underway. Manufacturers are creating working groups to improve expanded access,⁵ Reagan-Udall is working to facilitate the use of expanded access through its Expanded Access Navigator,⁶ and FDA is promoting the use of innovative trial designs, such as platform trials, to limit the need for

⁵Sandburg, B. (2020, January 23). Pharma Industry Broadens Its Approach To Expanded Access. Retrieved from <https://pink.pharmaintelligence.informa.com/PS141506/Pharma-Industry-Broadens-Its-Approach-To-Expanded-Access>

⁶ Expanded Access Navigator. (n.d.). Retrieved from <https://navigator.reaganudall.org/>

expanded access.⁷ NORD encourages Congress to build on these productive efforts and is grateful for the opportunity to comment on S. 3133. For questions regarding NORD or the above comments, please contact me at rsher@rarediseases.org, or 202-588-5700.

Sincerely,

A handwritten signature in black ink that reads "Rachel Sher". The signature is written in a cursive, flowing style.

Rachel Sher
Vice President, Policy and Regulatory Affairs

⁷ Cipriano, M. (2020, January 22). Platform Trials Could Be A Solution To Expanded Access, Woodcock Says. Retrieved from <https://pink.pharmaintelligence.informa.com/PS124614/Platform-Trials-Could-Be-A-Solution-To-Expanded-Access-Woodcock-Says>