



**Statement for the Record
National Organization for Rare Disorders**

**FDA User Fee Agreements: Advancing Medical Product Regulation
and Innovation for the Benefit of Patients
Senate Committee on Health, Education, Labor and Pensions
April 5, 2022**

Chairwoman Murray, Ranking Member Burr and members of the Health, Education, Labor and Pensions Committee, the National Organization for Rare Disorders (NORD) appreciates the opportunity to provide this statement for the record for the hearing “FDA User Fee Agreements: Advancing Medical Product Regulation and Innovation for the Benefit of Patients.”

Founded in 1983, NORD represents over 300 different rare disease patient organizations and the 25-30 million Americans living with a rare disease. We are committed to identifying, treating, and curing rare disorders through programs of education, policy, research, and patient services.

NORD appreciates the efforts of Congress, the FDA and negotiating parties in advancing strong User Fee Act commitment letters and the efforts to reauthorize the vital FDA User Fee Acts before their current authorization expires September 30, 2022. Despite substantial progress made possible by the passage of the Orphan Drug Act of 1983 and previous Prescription Drug User Fee Act (PDUFA) agreements, rare diseases remain an area with significant unmet need. Over 90% of the estimated 7,000 known rare diseases still do not have an FDA-approved treatment indicated for their specific rare disease.¹ Therefore, we support the approaches outlined in the PDUFA VII Commitment Letter to facilitate drug development, as well as timely review by FDA to ensure more treatment options are available to address the needs of rare disease patients.

NORD applauds the PDUFA VII Commitment Letter’s focus on the advancement of drug development for rare diseases. Sufficient staff resources at the FDA’s Center for Biologics Evaluation and Research (CBER) and Center for Drug Evaluation and Research (CDER) are critical to rare disease patients having timely access to FDA approved therapies. In recent years, there has been a dramatic rise in the number of investigational new drugs (INDs) received at CBER, driven in large part by advancements in cell and gene therapies^{2,3} and NORD is pleased

¹ Jennifer Huron, *New Study Investigates the Number of Available Orphan Products, Generics and Biosimilars*, Nat’l Org. for Rare Disorders (Mar. 25, 2021), <https://rarediseases.org/new-study-investigates-the-number-of-available-orphan-products-generics-and-biosimilars/>.

² Pink Sheet. Scientific Wave Pushes CBER Into Brighter Light. Accessed 10/1/21.

<https://pink.pharmaintelligence.informa.com/PS141927/Scientific-Wave-Pushes-CBER-Into-Brighter-Light>

³ RAPS. CBER lays out volume-staff mismatch in PDUFA VII meetings. Accessed 10/15/21.

<https://www.raps.org/news-and-articles/news-articles/2021/1/cber-lays-out-volume-staff-mismatch-in-pdufa-vii-m>

to see that under PDUFA VII, there are 228 planned CBER hires,⁴ a welcome increase of 196 more full-time employees (FTEs) than the 32 provided in PDUFA VI.⁵

CBER and CDER have committed to continuing the integration of rare disease staff into review divisions to ensure rare disease expertise is optimized throughout the review process. NORD believes this is a critical and constructive step. Rare diseases impact every system and part of the body, which means that any review division at the FDA may consider a rare disease application. Rare disease drug applications are often complex due to data collection challenges stemming from small patient populations. Additionally, the review of applications that rely on innovative methods to demonstrate the safety and effectiveness in rare disease drug development, such as the use of novel endpoints, adaptive study designs, and new methodologies for statistical analysis, requires the unique and collaborative approach envisioned in the Commitment Letter.

As part of PDUFA VII, the FDA has committed to incorporating rare disease training into the core curriculum for reviewers. Rare disease drug development poses unique challenges, such as small, heterogeneous patient populations and limited or non-existent natural history data, all of which can make endpoint selection difficult.^{6,7} Training that focuses on these challenges can help reviewers understand these applications, utilize regulatory flexibility as appropriate, and foster confidence in their ability to review rare disease products. Additionally, training can help to ensure that reviews are consistent across review divisions.

NORD also supports the establishment of the Rare Disease Endpoint Accelerator (RDEA) Pilot Program, which will provide critical resources to address novel endpoint development, a long-standing obstacle for rare disease drug development.^{8,9} As noted in the Commitment Letter, establishing appropriate efficacy endpoints in rare diseases is often challenging because of a lack of regulatory precedent, small trial populations, and limited understanding of a disease's natural history.¹⁰ The RDEA program will provide selected sponsors with an opportunity for earlier structured, repeated interactions with FDA to help in the evaluation and development of appropriate novel endpoints. In addition, NORD is pleased to see that FDA will consider the

⁴ FDA. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027. Page 59. (2021). Accessed 9/17/21. <https://www.fda.gov/media/151712/download>

⁵ FDA. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022. (2017). Accessed 9/17/21. <https://www.fda.gov/media/99140/download>

⁶ Golsmith, G., Kempf, L., Blumenrath, S. DIA. The Challenge of Rare Diseases – From Drug Development to Approval. Accessed 10/20/21. <https://globalforum.diaglobal.org/issue/april-2018/the-challenge-of-rare-diseases-from-drug-development-to-approval/>

⁷ FDA. Rare Diseases: Common Issues in Drug Development Guidance for Industry. (2019). <https://www.fda.gov/media/119757/download>

⁸ Raver, C, Valentine, J. FDA Law Blog. The FDA PDUFA VII Goals Letter (FY 2023-2027): A Review of Our Top 10 Commitments. Accessed 9/25/21. https://www.thefdalawblog.com/2021/09/the-fda-pdufa-vii-goals-letter-fy-2023-2027-a-review-of-our-top-10-commitments/?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+FdaLawBlog+%28FDA+Law+Blog%29

⁹ Pink Sheet. US FDA's Stein 'Excited' About Real-World Evidence, Rare Disease Endpoint Pilot Programs. Accessed 10/15/21. <https://pink.pharmaintelligence.informa.com/PS144943/US-FDAs-Stein-Excited-About-RealWorld-Evidence-Rare-Disease-Endpoint-Pilot-Programs>

¹⁰ FDA. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027. Page 30. (2021). Accessed 10/15/21. <https://www.fda.gov/media/151712/download>

applicability of the endpoints for multiple diseases, which will help broaden the impact of the pilot beyond the selected applicants.¹¹ It is critical that the learnings from this program ultimately be made available so that future rare disease drug applications can build on the progress made within the program.

The success of the RDEA program can be bolstered by the work being conducted in the Rare Disease Cures Accelerator-Data Analytics Platform (RDCA-DAP). Led collaboratively by the Critical Path Institute and NORD, the RDCA-DAP is an FDA-funded project that will create a widely available data resource, through which researchers and drug developers can access and analyze de-identified, patient-level data on rare diseases, and how they progress, leading to new insights about those diseases. The RDCA-DAP can provide potential drug development sponsors, even prior to the start of their own clinical studies, with access to (otherwise very hard to obtain) patient-level, rare disease data, and associated statistical analysis tools, that will allow sponsors to develop better proposals for the design and endpoints of their rare disease clinical trials. In so doing, the discussions with FDA during the RDEA consultation process can be improved. NORD encourages both sponsors and FDA to make full use of this resource in the RDEA Pilot.

Beyond the PDUFA VII Commitment Letter, NORD has identified several policy priorities for consideration as part of the PDUFA reauthorization that would help ensure a regulatory environment capable of addressing the tremendous unmet needs of the rare disease community.

Support Strengthening the Accelerated Approval Pathway

The accelerated approval pathway has proven to be a vital tool in bringing safe and effective treatments to patients with rare disorders. Many facets of rare diseases make them particularly difficult to study in clinical trials targeting direct clinical benefit. For example, the number of patients with a rare condition can be small and heterogeneous, with highly diverse clinical manifestations and a long timeframe for disease progression. Furthermore, there is often a lack of prior clinical studies and a limited number of clinical investigators and treatment centers knowledgeable about a given rare disorder. This makes accelerated approval, and the ability to use surrogate endpoints in the approval process, a particularly important tool for the development of treatments for rare diseases.¹²

However, the pathway faces mounting criticism from a variety of stakeholders who have raised concerns about the accelerated approval pathway. Critics of the accelerated approval pathway claim that these treatments have yet to demonstrate clinical benefit and should therefore be treated differently because they have been studied using surrogate endpoints and are not yet “clinically proven.” Some critics have characterized accelerated approval drugs as “experimental.” These criticisms of the accelerated approval pathway misunderstand the law and regulations that govern it.¹³ Accelerated approval—both as it is set forth in law and in

¹¹ FDA. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027. Page 31. (2021). Accessed 10/15/21. <https://www.fda.gov/media/151712/download>

¹² U.S. Food & Drug Admin., CDER Drug and Biologic Accelerated Approvals Based on a Surrogate Endpoint (Jan. 14, 2021), <https://www.fda.gov/media/88907/download>

¹³ 57 Fed. Reg. at 58944

regulations—does not alter FDA’s gold standard of substantial evidence of safety and effectiveness.¹⁴ To the contrary, accelerated approval is granted based on FDA’s finding that a drug is safe and effective for its intended use—the same approval standard used for traditional approval.¹⁵

Furthermore, Congress and the FDA have considered – and rejected – the notion that accelerated approval is a different or lesser standard than traditional approval. In fact, while codifying the accelerated approval pathway in 2012,¹⁶ Congress acknowledged the vital role the accelerated approval pathway serves for patients with rare diseases and expressed their hope that it would bring life-saving drugs to the market expeditiously.¹⁷ Congress also affirmed FDA’s conclusion that accelerated approval did not create a different standard for drug approval, stating in a “Sense of Congress” Congressional understanding that accelerated approval “may result in fewer, smaller, or shorter clinical trials... without compromising or altering the high standards of the FDA for the approval of drugs.”¹⁸

Still, NORD believes the accelerated approval pathway could benefit from certain reforms, that if implemented, would both help to alleviate payer concerns and support continued robust patient access to these FDA approved treatments. In a June 2021 white paper, FDA’s Accelerated Approval Pathway: A Rare Disease Perspective, NORD outlined several recommendations to improve the pathway.¹⁹ Such recommendations include:

Post-market Confirmatory Study Transparency

Post-market confirmatory studies are already a condition of accelerated approval but requiring more robust and frequent reports on manufacturers progress on their confirmatory studies would give all stakeholders more confidence that these confirmatory studies are being done with due diligence. Reports should compare actual progress on the milestones that the manufacturer agreed to at the time of accelerated approval and explain where progress is falling short of the agreement. The FDA should also be required to make the information contained within these reports easily accessible to the public by putting them on the FDA’s website.

Use of Real-World Evidence for Conversion to Traditional Approval

The FDA already utilizes real world evidence (RWE) in the post-market setting to evaluate safety and we believe that the utilization of RWE in the post-market to evaluate efficacy is often appropriate and should be considered. Consideration of RWE as part of the evaluation of whether the drug has an effect on the intended clinical benefit would permit FDA to convert accelerated approval drugs to traditional approval, when scientifically appropriate, at an earlier point in time.

¹⁴ 57 Fed. Reg. at 58944.

¹⁵ *Id.*

¹⁶ Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112–144, §§ 803, 901(b), 902(a), 126 Stat. 993, 1079, 1083–87 (2012)

¹⁷ See H.R. Rep. 112-495, *35–36 (2012)

¹⁸ See 158 Cong. Rec. H3825-01, H3848 (2012).

¹⁹ Temkin E, Trinh, J. FDA’s Accelerated Approval Pathway: A Rare Disease Perspective. October 2021.

https://rarediseases.org/wp-content/uploads/2021/06/NRD-2182-Policy-Report_Accelerated-Approval_FNL.pdf

Expedited Withdrawal of an Accelerated Approval Product

It can be difficult to design, enroll, and complete post-marketing confirmatory studies for rare disease drugs and there are frequently legitimate reasons for delays in converting a product from accelerated approval to traditional approval. However, delayed confirmatory studies also give fodder to critics of accelerated approval who claim they are a result of an inability by FDA to properly address or enforce action against accelerated approval products that have not proven clinical benefit. Clarifying the circumstances under which the expedited withdrawal of an accelerated approval product would be appropriate is important for building confidence in the pathway. However, it is also critical that some flexibility be retained by the FDA in the event sponsors are pursuing conversion to traditional approval with due diligence but are falling behind on established milestones and targets.

Increased Funding and Resources for FDA

Many of these proposals would require additional, targeted resources at FDA. An increase in federal funding and resources through budgeting and appropriations could provide FDA with the resources necessary to implement some of the reforms contemplated and to exercise its existing and ideally expanded authorities when appropriate.

FDA approval is only the first step to a patient obtaining access to a treatment. True access is achieved when patients can get their treatments prescribed and affordably covered by their health program or insurer. Ongoing concerns about continued patient access to products approved via accelerated approval are why 89 patient organizations joined NORD in sending a letter to Senate HELP and House Energy and Commerce Committee Chairs and Ranking Members urging them to incorporate the policy recommendations referenced above into legislation to reauthorize PDUFA in order to strengthen the AA pathway and facilitate patient access to rare disease therapies. A copy of this letter is included at the end of this statement.

NORD looks forward to working with Congress to ensure this pathway remains a viable way for patients to obtain access to FDA approved treatments for their rare condition at the earliest possible time.

Support Optimizing Patient Focused Drug Development

NORD appreciates that the PDUFA VII Commitment Letter continues FDA's focus on incorporating the patient voice into the drug development and regulatory review processes. Through our work assisting Member Organizations planning several externally-led Patient-Focused Drug Development (EL-PFDD) meetings, and our own work directly coordinating several EL-PFDDs, NORD has seen firsthand the transformative impact for the patient communities in hosting PFDDs. Patients are the ultimate experts of their disease because they live with it every day. NORD welcomes provisions in the Commitment Letter to increase the utilization of PFDD, including the draft guidance on the use and submission of patient preference information for regulatory decision making. Currently, patient data is inconsistently collected and can have limited value in regulatory decision making. Changing this paradigm to ensure robust, fit-for purpose patient data is consistently collected will increase the value and utility of patient data within the FDA review process.

Support Expanding Clinical Trial Diversity

Ensuring that clinical trials appropriately represent the intended patient populations is priority for NORD. This is a critically important issue and can be a challenge with rare diseases as they usually have much smaller clinical trials due to the limited number of eligible patients.

Many different issues – including geographic, linguistic, cultural, and socio-economic factors – exist that tend to reduce diversity in clinical trials and lead to unfortunate inequities for patients. The NORD Rare Disease Centers of Excellence program consciously aims to address those factors, to make clinical trial enrollment easier and more equitable. The network features 31 sites in multiple states, which should present patients with opportunities to enroll in clinical trials closer to their homes and serve diverse populations in a variety of regional settings. Many of the centers already have experience and programs devoted to reaching out to medically underserved communities in their region, enabling us to reach patients with a variety of backgrounds, such as:

- Black communities, both urban and rural, who may have a strong mistrust of clinical research due to historical and sadly even more recent unethical medical research.
- New immigrants and undocumented immigrant communities who, in addition to language and medical coverage barriers, may fear exposing themselves or family members to a perceived risk of increased scrutiny by US Citizenship and Immigration Services.
- Rural communities who tend to have a lower socio-economic status, limited access to health care facilities and/or to health insurance.

To increase the chances of overcoming these challenges regardless of where in our country a patient is located, NORD intends to identify best practices for community outreach and for equitable clinical enrollment at the centers where such practices have already been developed. We will share those best practices across all the centers, to increase the ease and the diversity of enrollment in clinical trials across the network and throughout the country.

Conclusion

Chairwoman Murray and Ranking Member Burr, thank you for the opportunity to submit this statement for the record and for your efforts to ensure the FDA has the resources and oversight it needs to review and approve new and innovative therapies for rare disease patients. NORD looks forward to working with you and your staff to see PDUFA VII and the other critical FDA user fee acts reauthorized in a timely manner and effectively implemented to benefit the rare disease community. For more information, please contact Heidi Ross, Acting Vice-President of Policy and Regulatory Affairs at HRoss@rarediseases.org.



April 4, 2022

The Honorable Patty Murray
Chairwoman
Committee on Health, Education, Labor & Pensions
United States Senate
Washington, D.C. 20510

The Honorable Richard Burr
Ranking Member
Committee on Health, Education, Labor & Pensions
United States Senate
Washington, D.C. 20510

The Honorable Frank Pallone
Chairman
Committee on Energy and Commerce
United States House of Representatives
Washington, D.C. 20515

The Honorable Cathy McMorris Rodgers
Ranking Member
Committee on Energy and Commerce
United States House of Representatives
Washington, D.C. 20515

Dear Chairwoman Murray, Ranking Member Burr, Chairman Pallone, and Ranking Member McMorris Rodgers,

The 91 undersigned organizations, representing patients with rare diseases and other acute or chronic health conditions, urge you to include as part of this year's Prescription Drug User Fee Act (PDUFA) reauthorization provisions to strengthen the Food and Drug Administration's (FDA) accelerated approval (AA) pathway and enable patient access to these critical, often life-saving therapies. The AA pathway has proven itself to be a vital tool in bringing safe and effective treatments to many patients, including those with rare diseases. However, the pathway faces mounting criticism from a variety of stakeholders.¹ Some of these concerns have led to several proposals now before the Department of Health and Human Services (HHS) for consideration, that if approved and implemented, would undermine the authority of the FDA and delay or potentially bar patients from accessing crucial therapies where no other options exist.^{2 3} While there are legitimate criticisms of the AA pathway, too often it appears that issues with accelerated approval are being used as a proxy for the broader health system's challenges with high prescription drug costs. Reducing patient access to therapies that utilize a specific FDA pathway will not solve problems with accelerated approval or prescription drug costs. Therefore, we urge Congress to incorporate into PDUFA reauthorization several recommendations outlined with this letter to strengthen the AA pathway and facilitate patient access to rare disease therapies that utilize accelerated approval.

The History and Importance of Accelerated Approval to the Rare Disease Community

The AA pathway was first enshrined in regulation in 1992, after the HIV/AIDS epidemic had drastically altered the landscape for drug development.⁴ In response to the epidemic, scientists sought ways to streamline and expedite clinical trials for HIV/AIDS drugs to focus on the utility of surrogate endpoints which were known to demonstrably correlate with improved outcomes.⁵ As consensus grew about the utility of surrogate endpoints in clinical trial design, FDA embraced drug approval reform and promulgated regulations formalizing the AA pathway.⁶ Under accelerated approval, the time required to receive FDA approval was considerably shortened allowing for earlier patient access to drugs that were intended to treat serious and life-threatening diseases and conditions for which there were unmet medical needs, including many rare diseases.

¹ Medicaid and CHIP Payment and Access Commission (MACPAC), *Report to Congress on Medicaid and CHIP*, June 2021, <https://www.macpac.gov/wp-content/uploads/2021/06/June-2021-Report-to-Congress-on-Medicaid-and-CHIP.pdf>

² Oregon Health Authority, *2022-2027 Medicaid 1115 Demonstration Application*, (February 18, 2022), <https://www.oregon.gov/oha/HSD/Medicaid-Policy/Documents/2022-2027-Waiver-Application-Final.pdf>

³ Centers for Medicare & Medicaid Services, *Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (CAG-00460N)*, (January 11, 2022), <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&NCAId=305>

⁴ The Centers for Disease Control and Prevention ("CDC") published its first report on HIV/AIDS in 1981. See James W. Curran & Harold W. Jaffe, AIDS: The Early Years and CDC's Response, 60 *Morbidity & Mortality Weekly Rep.* 64 (Oct. 7, 2011), available at <https://www.cdc.gov/mmwr/preview/mmwrhtml/su6004a11.htm>.

⁵ See U.S. Food & Drug Admin., *Guidance for Industry: Human Immunodeficiency Virus-1 Infection: Developing Antiretroviral Drugs for Treatment 3* (Nov. 2015), www.fda.gov/files/drugs/published/Human-Immunodeficiency-Virus-1-Infection--Developing-Antiretroviral-Drugs-for-Treatment.pdf

⁶ FDA also created the fast track, breakthrough therapy, and priority review designations to advance the development and review of new drugs and address unmet needs in the treatment of a serious medical condition. See U.S. Food & Drug Admin., *Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics 1* (May 2014) ("Expedited Programs Guidance"), <https://www.fda.gov/media/86377/download>

It is estimated that 25-30 million Americans (or 1 in 10 individuals) suffer from rare diseases, which are typically serious and life-threatening conditions with unmet medical needs.⁷ Of the 7,000 rare diseases that have been identified, more than 90% have no FDA-approved treatment.⁸ Many facets of rare diseases make them particularly difficult to study in clinical trials targeting direct clinical benefit. For example, the number of patients with any one condition can be small and heterogeneous, with highly diverse clinical manifestations and a long timeframe for disease progression. Furthermore, there is often a lack of prior clinical studies and a limited number of clinical investigators and treatment centers knowledgeable about a given rare disorder.⁹ This makes accelerated approval, and the ability to use surrogate endpoints in the approval process, a particularly important tool for the development of treatments for rare diseases.¹⁰

Threats to the Accelerated Approval Pathway

Increasingly, the AA pathway, and products that utilize the pathway, are being targeted for differential treatment by various payers in the health care system.¹¹

- Institute for Clinical and Economic Review (ICER) and the Medicaid and CHIP Payment and Access Commission (MACPAC) have both advocated for an increase in mandatory federal rebates for accelerated approval drugs until their confirmatory studies are complete and are granted traditional approval.^{12 13}
- Centers for Medicare and Medicaid Services (CMS) has proposed to cover an entire drug class, monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease, under Coverage with Evidence Development (CED).¹⁴
- Oregon, as part of their Medicaid 1115 waiver proposal, has requested permission from CMS to exclude Medicaid "coverage of accelerated approval drugs with limited or inadequate evidence of clinical efficacy".¹⁵

Many critics of the AA pathway claim that these treatments have yet to demonstrate clinical benefit and should therefore be treated differently because they have been studied using surrogate endpoints and are not yet "clinically proven."¹⁶ Furthermore, critics have characterized accelerated approval drugs as "experimental." These criticisms of the AA pathway misunderstand the law and regulations that govern it. Surrogate endpoints are chosen because FDA, in its scientific discretion, has determined they are reasonably likely to predict clinical benefit. Accelerated approval—both as it is set forth in law and in regulations—does not alter FDA's gold

⁷ Jennifer Huron, *New Study Investigates the Number of Available Orphan Products, Generics and Biosimilars*, Nat'l Org. for Rare Disorders (Mar. 25, 2021), <https://rarediseases.org/new-study-investigates-the-number-of-available-orphan-products-generics-and-biosimilars/>.

⁸ *Id.*

⁹ Food and Drug Administration. Report: Complex Issues in Developing Drugs and Biological Products for Rare Diseases and Accelerating the Development of Therapies for Pediatric Rare Diseases Including Strategic Plan: Accelerating the Development of Therapies for Pediatric Rare Diseases. July 2014. <https://www.fda.gov/media/89051/download>

¹⁰ U.S. Food & Drug Admin., CDER Drug and Biologic Accelerated Approvals Based on a Surrogate Endpoint (Jan. 14, 2021), <https://www.fda.gov/media/88907/download>

¹¹ The undersigned organizations may or may not have taken positions on the individual proposals listed below and include them only as context for ongoing discussions on AA.

¹² Institute for Clinical and Economic Review (ICER), *Strengthening the Accelerated Approval Pathway: An Analysis of Potential Policy Reforms and their Impact on Uncertainty, Access, Innovation, and Costs*, (April 26, 2021) <https://icer.org/wp-content/uploads/2021/04/Strengthening-the-Accelerated-Approval-Pathway--ICER-White-Paper--April-2021.pdf>

¹³ MACPAC, *supra* note 1

¹⁴ Centers for Medicare & Medicaid Services, *supra* note 3

¹⁵ Oregon Health Authority, *supra* note 2

¹⁶ *Id.*

standard of substantial evidence of safety and effectiveness.¹⁷ To the contrary, accelerated approval is granted based on FDA's finding that a drug is safe and effective for its intended use—the same approval standard used for traditional approval. Furthermore, Congress and the FDA have considered – and rejected – the notion that accelerated approval is a different or lesser standard than traditional approval.¹⁸

Recommendations to Strengthen the Accelerated Approval Pathway

FDA approval is only the first step to a patient obtaining access to a treatment. True access is only achieved when patients receive treatments prescribed and affordably covered by their health program or insurer. Too often this is a serious challenge for rare disease patients. Treating products that utilize accelerated approval differently will not solve these patient access challenges. Therefore, we urge you to focus on advancing legislation to strengthen the pathway and believe the following proposals would do just that while simultaneously alleviating payer concerns and without compromising robust patient access.

Post-market Confirmatory Study Transparency

Post-market confirmatory studies are already a condition of accelerated approval but requiring more robust, frequent, and transparent reports on the design of confirmatory studies and a manufacturers progress on their confirmatory studies would give all stakeholders more confidence that studies are being completed with due diligence. Reports should compare realized progress on the milestones that the manufacturer agreed to at the time of accelerated approval and explain where progress is falling short of the agreement. The FDA should also be required to make this information easily accessible to the public by publishing it on the FDA's website in a timely manner.

Use of Real-World Evidence for Conversion to Traditional Approval

The FDA already utilizes real world evidence (RWE) in the post-market to evaluate safety, and our organizations believe that the FDA should consider, when appropriate, RWE in the post-market in evaluations intended to confirm efficacy in products approved through accelerated approval. Consideration of RWE as part of the evaluation of whether the drug has an effect on the intended clinical benefit would permit FDA to convert accelerated approval drugs to traditional approval, when scientifically appropriate, at an earlier point in time.

Expedited Withdrawal of an Accelerated Approval Product

It can be difficult to design, enroll, and complete post-marketing confirmatory studies for rare disease drugs and there are frequently legitimate reasons for delays in converting a product from accelerated approval to traditional approval. However, delayed confirmatory studies extend prescriber and patient uncertainty and also give fodder to critics of accelerated approval who point to them as evidence that FDA doesn't have the ability to properly address or enforce action against accelerated approval products that have not proven clinical benefit. Establishing clear circumstances under which the expedited withdrawal of an accelerated approval product would be appropriate is important for holding drugmakers accountable for timely completion of confirmatory studies and building confidence in the pathway.

¹⁷ 57 Fed. Reg. at 58944

¹⁸ See 158 Cong. Rec. H3825-01, H3848 (2012).

Increased Funding and Resources for FDA

Many of the ideas proposed herein would require additional, targeted resources at FDA. An increase in federal funding and resources through budgeting and appropriations could provide FDA with the resources necessary to implement some of the reforms contemplated and to exercise its existing and ideally expanded authorities when appropriate.

Conclusion

Accelerated approval is critical to the innovation and development of new drugs to treat rare diseases. Our organizations believe these reforms will result in an efficient and transparent use of the AA pathway so that all stakeholders have confidence in products that come onto the market through accelerated approval.

We urge Congress to advance legislation that supports timely patient access to treatments that have been FDA approved through the accelerated approval pathway and strengthens FDA's authority and crucial role in making sure safe and effective drugs are available to improve the health of all people, including those with rare diseases, in the United States. For more information, please contact Heidi Ross, Acting Vice-President of Policy and Regulatory Affairs at the National Organization for Rare Disorders, at HRoss@rarediseases.org.

Thank you for your consideration,

National Organization for Rare Disorders
Alport Syndrome Foundation
ALS Association
American Kidney Fund
Angelman Syndrome Foundation
Angioma Alliance
Arthritis Foundation
Asbestos Disease Awareness Organization
Association for Creatine Deficiencies
Avery's Hope
CACNA1A Foundation
CDG CARE
Child Neurology Foundation
Choroideremia Research Foundation
Conquering Gyrate Atrophy
CSNK2A1 Foundation
Cure CMD
Cure HHT
CureCMT4J
CURED Nfp
Cystic Fibrosis Research Institute (CFRI)
DCM Foundation
Dreamsickle Kids Foundation, Inc
Dup15q Alliance
Epilepsy Foundation

Fabry Support & Information Group
FACES; The National Craniofacial Association
FOD Family Support Group
Foundation for Sarcoidosis Research
Free ME from Lung Cancer
Galactosemia Foundation
Gaucher Community Alliance
Global Healthy Living Foundation
Gorlin Syndrome Alliance
Greater Boston Sickle Cell Disease Association
GRIN2B Foundation
HCU Network America
Hemophilia Federation of America
Hepatitis B Foundation
Hereditary Neuropathy Foundation
Hermansky-Pudlak Syndrome Network
Huntington's Disease Society of America
Huntington's Disease Youth Organization
Hydrocephalus Association
IGA Nephropathy Foundation
Immune Deficiency Foundation
International Foundation for Autoimmune &
Autoinflammatory Arthritis (AiArthritis)
International Foundation for CDKL5 Research
International Pemphigus Pemphigoid Foundation

International Waldenstrom's Macroglobulinemia
Foundation
JDRF
Lupus Foundation of America
Malan Syndrome Foundation
M-CM Network
MdDS Balance Disorder Foundation
MPN Advocacy & Education International
Muscular Dystrophy Association
National Median Arcuate Ligament Syndrome
Foundation Inc
National Multiple Sclerosis Society
National Patient Advocate Foundation
National PKU Alliance
National PKU News
NBIA Disorders Association
NephCure Kidney International
No Stomach For Cancer
NTM Info & Research
Phelan-McDermid Syndrome Foundation
Pulmonary Fibrosis Foundation
Recurrent Respiratory Papillomatosis Foundation

Remember The Girls
RETpositive Inc.
Ring14 USA
SATB2 Gene Foundation
SCID Angels for Life
Sickle Cell Reproductive Health Education Directive
SLC6A1 Connect
STXBP1 Foundation
SYNGAP1 Foundation
The Akari Foundation
The AKU Society of North America
The Association for Frontotemporal Degeneration
The Leukemia & Lymphoma Society
The Life Raft Group
The Patient Story
The RYR-1 Foundation
United Leukodystrophy Foundation
Upstage Lung Cancer
Vasculitis Foundation
VHL Alliance
Williams Syndrome Association
Xia-Gibbs Society, Inc.

CC:

The Honorable Tammy Baldwin, Chair Agriculture Appropriations Subcommittee, U.S. Senate
The Honorable John Hoeven, Ranking Member Agriculture Appropriations Subcommittee, U.S. Senate
The Honorable Sanford Bishop, Chair Agriculture Appropriations Subcommittee, U.S. House of Representatives
The Honorable Andy Harris, Acting Ranking Member Agriculture Appropriations Subcommittee, U.S. House of Representatives