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CONSUMERS FOR HEALTH CARE CHOICES

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How Extending the AIDS Drug Access Model to Other Diseases Would Save Lives

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Summary

- In the 1980s, the AIDS/HIV epidemic gave rise to a political movement that forced the creation of a "parallel track" to expedite the slow-moving Food and Drug Administration certification process.
- This parallel track provided quicker access to life-saving drugs for AIDS/HIV patients.
- In the following years, the FDA created other paths to expedite new drug approval, but none with the promise offered by the parallel track.
- Free to Choose Medicine would build on the parallel track reforms and potentially extend the option to all new drugs.

Executive Summary

Millions of Americans suffer and even die each year because they lack access to the most effective medications needed to treat their ailments. A principal bottleneck to getting drugs to such patients is the U.S. Food and Drug Administration (FDA). That government agency is required by law to certify the safety and efficacy of all drugs before they can be made widely available to patients, and it often fails to make treatments available in a timely manner, leaving countless patients suffering while they wait for government approval. It currently takes on average 10 to 12 years and as much as $2.6 billion to bring a new treatment from the research lab to patients—and much of that time is spent satisfying government requirements.[1]

However, more than two decades ago, FDA began to make some significant, albeit limited, reforms. The AIDS/HIV epidemic, which began in the early 1980s, had afflicted hundreds of thousands of people by 1992. Tens of thousands were dying each year. For sufferers, waiting for pharmaceutical companies to complete FDA's years-long process to approve new treatments was not an option. Patients and activists pushed for change, and as a result, an alternative "parallel track" was

[1] "How the Tufts Center for the Study of Drug Development Pegged the Cost of a New Drug at $2.6 Billion," Tufts Center for the Study of Drug Development, November 18, 2014. https://static1.squarespace.com/static/5a9eb0c8e2ccd1158288d8dc/t/5ac66aeb0e2e7280a329b092/1522952939855/cost_study_backgrounder.pdf.

devised that allowed AIDS/HIV sufferers to more quickly have access to treatments that saved and extended lives and offered drug developers an added incentive to invest in new treatments.

Despite general reforms instituted in the years that followed, FDA continues to operate inefficiently, as evidenced by the still-lengthy wait times required for certification and the ever-increasing costs of new drugs. When the parallel track was created for AIDS/HIV treatments, many sought to have the same option extended to help those suffering with other ailments. Federal policymakers, however, chose not to do so. Instead, they created partial measures that only applied in very specific situations but did not offer the more open and innovative approach of parallel track. After AIDS/HIV treatments were quickly developed and approved—thanks in large part to the pressure from patients and reform advocates—the parallel track option was not used again for a number of reasons, including the fact that it did not go far enough.

Hundreds of thousands are afflicted with a long list of debilitating diseases—Alzheimer's, ALS, Parkinson's, cancers of various kinds—with tens of thousands dying each year. Patients suffering from these diseases, along with their families, friends, and caretakers, are right to ask why a quicker, more streamlined process similar to parallel track is not available to them as well.

The political will is emerging to create a drug approval system that will offer an opportunity to expedite access to potentially life-changing, life-saving drugs and treatments. President Donald Trump has called for a major commitment to eliminating AIDS/HIV and childhood cancer.[2] Members of both parties are looking for ways to contain rising drug prices. Meeting these important goals will not require increasing the size of the federal budget. Instead, there must be a substantial decrease in the number of federal regulations.

THIS *POLICY BRIEF* WILL OUTLINE THE NEED TO SPEED UP TREATMENTS AND CURES FOR THESE AND OTHER DISEASES, WHICH IS AS CRITICAL NOW AS THE NEED TO FACILITATE THE DEVELOPMENT AND DELIVERY OF MEDICATIONS FOR AIDS/HIV SUFFERERS WAS THREE DECADES AGO.

This *Policy Brief* will outline the need to speed up treatments and cures for these and other diseases, which is as critical now as the need to facilitate the development and delivery of medications for AIDS/HIV sufferers was three decades ago. Further, it will show the best option is to enact Free to Choose Medicine, which would take the AIDS/HIV parallel track option much further, helping to usher in a truly golden age of medicine and innovative cures.

[2] "Remarks of President Trump in State of the Union Address," State of the Union Address, WhiteHouse.gov, February 5, 2019, https://www.whitehouse.gov/briefings-statements/remarks-president-trump-state-union-address-2/

The paper will consider the following:

1. Improving Safety, Efficacy, and Access

With its origins nearly a century ago, FDA was initially designed to protect the public from dangerous "snake oil" medicines. In the years since, FDA's mandate has expanded beyond certifying safety to demonstrating efficacy beyond a reasonable doubt. The wait times and costs it has placed on developing new treatments has, in many instances, kept safe and effective medications from patients, costing thousands of lives and untold billions of dollars in unnecessary health care costs.

2. The AIDS/HIV Epidemic

The AIDS/HIV epidemic gave rise to an effective political movement that forced the federal government to facilitate an alternative to the time-consuming FDA approval process. As a result, in the 1990s, the Public Health Service proposed and adopted a policy for expanding access to AIDS/HIV drugs and treatments.

3. A Parallel Track to Treatment

In 1992, the AIDS/HIV "parallel track" was approved as a regulatory change for FDA to allow patients exclusive access to AIDS/HIV drugs that had passed safety tests but had not yet passed all efficacy tests. Other drugs did not have access to this approval option. As a result of parallel track, the highly effective anti-viral drug stavudine was approved, saving thousands of lives.

4. Complex Paths to Expedite Drug Approval

In the years that followed, FDA and Congress created several paths to speed approval and open access to promising medications, including accelerated approval, priority review, fast track, breakthrough therapy, right to try, and expanded access, or "compassionate use." Unfortunately, these approaches are often confusing, and it is difficult for drug developers to determine which approach to pursue. None of these reforms have matched the openness and simplicity of the parallel track, and they have failed to eliminate the unnecessarily long waits and high costs that continue to plague most of FDA's approval process. They have also failed to place the principal decision-making concerning treatments in the hands of patients and their doctors.

5. The Free to Choose Medicine Solution

Today, many ailments—for example, Alzheimer's—cause debilitation, suffering, and even death in a manner similar to what AIDS/HIV patients faced in the past, both in terms of total economic cost and number of sufferers. Free to Choose Medicine is like the parallel track, but it includes critical, sensitive improvements: First, drug manufacturers decide whether to offer a product on the parallel track. Second, any patient, in consultation with a physician, can access the product. Third, FTCM creates a Tradeoff Evaluation Drug Database, which would provide real-world data in addition to clinical trials that would allow product efficacy to be gauged.

6. The Path to FTCM

FTCM could be implemented in the same way parallel track received approval, through a regulatory change, rather than act of Congress. But for this to occur, reformers both inside and outside of FDA, and patients most of all, need to adopt the same sense of urgency employed by AIDS/HIV activists in their fight to compel FDA to adopt parallel track.

> While no one disputes medicines should be safe and efficacious, having medications available in a timely manner to alleviate suffering and save lives is also crucial.

1. Improving Safety, Efficacy, and Access

The Food and Drug Administration originated in 1927 as an agency meant to protect the public from adulterated or mislabeled drugs and "snake oil" medicines. In 1937, the Federal Food, Drug, and Cosmetic Act expanded its powers, authorizing FDA to certify the safety of drugs before they could be marketed and to classify some drugs as "prescription only." In 1959, the drug thalidomide was misused in Europe, causing thousands of birth defects. While that product was stopped from use in the United States, Congress, in 1962, passed the Kefauver-Harris Amendments in reaction to the thalidomide issue in Europe. The Kefauver-Harris Amendments gave FDA even more authority, this time not only requiring safety testing, but now also rigorous efficacy testing before products could be marketed.[3]

In the two decades that followed, FDA grew overly cautious, according to numerous scholars and policymakers. Dale H. Gieringer observed, "By 1976 the cost of developing a new drug had risen to an estimated $24 million, 10 to 20 times as much as in the early 1960s, while development times had climbed from a couple of years to the better part of a decade."[4,5]

These costs and delays cost human lives.[6] For example, "Beta blockers regulate hypertension and heart problems. The FDA held up approval for eight years because it believed they caused cancer. In the meantime, according to

[3] Public Law 87-781~OCT. 10,1962, p. 780. https://prescriptiondrugs.procon.org/sourcefiles/1962Amendments.pdf; Also see "Kefauver-Harris Amendments Revolutionized Drug Development," FDA Consumer Health Information, October, 1992, https://www.gvsu.edu/cms4/asset/F51281F0-00AF-E25A-5BF632E8D4A243C7/kefauver-harris_amendments.fda.thalidomide.pdf

[4] Note that $24 million would be $122 million in 2018 dollars. A Tufts estimate puts today's cost of bringing a new product from lab to market at $2.6 billion.

[5] Dale H. Gieringer, "The Safety And Efficacy Of New Drug Approval," *The Cato Journal*, Volume 5, Number 1 (Spring/Summer 1985), p. 178, https://pdfs.semanticscholar.org/feb9/53ab293f24a14b3b3d4b748281420099b4b1.pdf; Also see WM Wardell et al., "The rate of development of new drugs in the United States, 1963 through 1975," *Clin Pharmacol Ther.*, August 1978, Volume 24, Issue 2, pp. 133–145, https://www.ncbi.nlm.nih.gov/pubmed/679593

[6] *Ibid*., p. 190.

Dr. Louis Lasagna of Tufts University, 119,000 people died who might have been helped by the medication."[7] During most of that period, beta blockers were available in Europe. This led to a *Wall Street Journal* headline titled, "100,000 killed."[8]

While no one disputes medicines should be safe and efficacious, having medications available in a timely manner to alleviate suffering and save lives is also crucial. FDA, as it does now, erred too much on the side of caution, often endangering rather than protecting lives.

There were no confirmed cases or deaths at the start of the decade, but by 1992, new reported AIDS cases reached 75,457 per year and annual deaths topped 50,600 in 1995.

2. The AIDS/HIV Epidemic

It was in the context of this slow, bureaucratic FDA the AIDS/HIV epidemic emerged in the 1980s. There were no confirmed cases or deaths at the start of the decade, but by 1992, new reported AIDS cases reached 75,457 per year and annual deaths topped 50,600 in 1995.[9] In one year, nearly as many Americans died because of AIDS/HIV than the number of Americans killed in the Vietnam War. Because this was a new ailment, there were no known cures or effective treatments.

Emblematic of its early failure to take the epidemic seriously and cut through its own red tape, FDA proposed classifying a home testing kit for the HIV virus—essentially a cup for holding a urine specimen that would be sent to a lab—as a Class 3 medical device, the same category as heart valves. A U.S. Court of Appeals rejected this classification, but even more was needed to force FDA to put patients first.[10]

Because of the high HIV mortality rate, sufferers refused to wait on the slow FDA bureaucracy. They developed their own networks to exchange information about which treatments looked most promising.

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[7] Victor Niederhoffer and Laurel Kenner, *Practical Speculation*, Wiley, May 2008, p. 306, https://books.google.com/books?id=wJ8iLx1rBJUC&pg=PA306&lpg=PA306&dq=Interleukin+2+delay+Lasagna&source=bl&ots=sS-bXjYuKA&sig=sJwNJQE32MYO3Q5j3G3R7uKo1mk&hl=en&sa=X&ved=2-ahUKEwjWodr86fLfAhWPxVkKHYcMBYoQ6AEwCHoECAYQAQ#v=onepage&q=Interleukin%202%20delay%20Lasagna&f=false

[8] "100,000 Killed," *The Wall Street Journal*, November 2, 1981, p. 26.

[9] "HIV Surveillance—1981-2008," *Morbidity and Mortality Weekly Report*, Centers for Disease Control and Prevention, Volume 60, Issue No. 21, June 3, 2011, https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6021a2.htm?s_cid=mm6021a2_w

[10] Edward Hudgins, "Kessler's FDA: An Autopsy," *Regulation* magazine, Volume 1, 1997, https://object.cato.org/sites/cato.org/files/serials/files/regulation/1997/1/reg20n1.html#PERSPECTIVE_2. Also see "Clinical Reference Laboratory Challenges FDA Efforts to Regulate HIV Testing for Insurance Industry," *Biotechnology Law Report*, Vol. 11, No. 1, January-February 1992. https://www.liebertpub.com/doi/abs/10.1089/blr.1992.11.12?journalCode=blr

The 2013 Oscar-winning film *Dallas Buyers Club* portrayed AIDS/HIV sufferers smuggling and distributing drugs unapproved by the FDA to treat their symptoms. An alliance of activist groups organized to raise awareness of the disease and took political action.[11] In 1988, thousands demonstrated at FDA headquarters in Maryland.[12] They pushed every political button they could. Rep. Henry Waxman (D-CA) successfully sponsored the "Ryan White CARE Act" to provide financial assistance to AIDS/HIV victims. Waxman, whose Los Angeles-area district contained one of the largest populations of AIDS/HIV sufferers, was instrumental in raising consciousness about the disease, pushing the Department of Health and Human Services and FDA to create an expedited certification system.

The federal bureaucracy finally got the message. On May 21, 1990, the Public Health Service (PHS), the division of HHS under which FDA operates, announced in the *Federal Register* and sought public comments "on a proposed policy to make promising investigational drugs for AIDS and HIV-related diseases more widely available under 'parallel track' protocols."[13] The posting acknowledged that "persons with other life-threatening diseases might also wish to have investigational drugs available through a parallel track mechanism."[14] But it singled out those individuals suffering from AIDS/HIV "for whom there are no wholly satisfactory therapies." It identified the parallel track as "a pilot effort, therefore it is preferable to work out the procedures and to evaluate its operation," presumably before extending it to other illnesses. (Free to Choose Medicine has worked out procedures and perfected the concept behind the parallel track. See Section Five below.)

It also noted that "based on the interactions with patient advocacy groups (e.g., National Association of People with AIDS, The AIDS Coalition to Unleash Power and Project Inform) and physicians specializing in the care of HIV-infected individuals, there exists willingness among HIV-infected persons to participate in clinical studies as well as an expanded availability program." The origin of the parallel track was pressure from such groups and individuals. The deadline to submit comments was July 20, 1990, two months after the announcement of the intended new policy.

It was significant that the PHS and FDA did not need congressional legislation to create a parallel track. FDA considered this action to be within its own grant of authority to determine how best to meet its mandate to ensure safety and efficacy. This claim to authority was not a point of dispute. Most comments, reviewed below, concerned the particulars about how such a track might operate or its

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[11] Douglas Crimp, "Before Occupy: How AIDS Activists Seized Control of the FDA in 1988," *The Atlantic*, December 6, 2011, https://www.theatlantic.com/health/archive/2011/12/before-occupy-how-aids-activists-seized-control-of-the-fda-in-1988/249302

[12] Warren E. Leary, "F.D.A. Pressed to Approve More AIDS Drugs," *The New York Times*, October 11, 1988, https://www.nytimes.com/1988/10/11/science/fda-pressed-to-approve-more-aids-drugs.html

[13] *Federal Register*, Volume 55, Issue No. 96, May 21, 1990, p. 20,856. https://cdn.loc.gov/service/ll/fedreg/fr055/fr055098/fr055098.pdf

[14] *Ibid.*

overall wisdom. This administrative approach to reform can be considered a precedent and is a significant point for those seeking FDA reform today.

3. A Parallel Track to Treatment

Perhaps also emblematic of the problems with FDA, it wasn't until April 15, 1992—two years after the solicitation of input on the parallel track—that the PHS and FDA announced in the *Federal Register* the results of that solicitation and the intention to adopt the parallel track.[15] That track allowed access for AIDS/HIV suffers to drugs that had not gone through the full FDA certification process.

THE ENTIRE PROCESS CAN TAKE A DECADE, AND, AT BEST, A FEW THOUSAND INDIVIDUALS CAN HAVE ACCESS TO PROMISING DRUGS WHILE PARTICIPATING IN CLINICAL TRIALS.

The routine FDA certification process normally begins with drug developers, manufacturers, or sponsors submitting what they hope will be an effective medication to Phase I basic safety tests, which usually involves about 20–100 volunteers. Safe and promising drugs go on to Phase II clinical trials, which can involve as many as 500 patients and seek to determine a trial drug's general efficacy and side effects. Phase III refines information about the product and its dosages; it can involve several thousand patients.[16] During the standard randomized clinical tests required in these latter phases, usually half the test participants receives the medication under review while the other half receives placebos. After these three phases are complete, manufacturers can submit a New Drug Application to FDA, which then decides whether to approve the product.

The entire process can take a decade, and, at best, a few thousand individuals can have access to promising drugs while participating in clinical trials. With hundreds of thousands suffering and dying from AIDS/HIV in the 1980s, an alternative was needed.

Clinical Trials Controversy

The 1992 *Federal Register* post began with a review of the comments about the proposed parallel track.[17] A crucial controversy reflected in both the comments and the plan itself concern the "Impact of Parallel Track on Clinical Trials." Specifically, "Some comments suggested that parallel track studies should be delayed for a period of time to allow for Phase 2 controlled trial accrual. One comment stated that the controlled trial enrollment should be completed before a drug is made available

[15] *Federal Register*, Volume 57, Issue No. 73, April 15, 1992, p. 13,250–13,259. https://cdn.loc.gov/service/ll/fedreg/fr057/fr057073/fr057073.pdf

[16] Bartley J. Madden, *Free to Choose Medicine*, Third Edition (Arlington Heights, IL: The Heartland Institute, 2017), p. 20.

[17] The *Federal Register*, Volume 57, summarized in response to the initial solicitation of input, "1,210 comments were received; of these, 200 were unique while the other 1,010 were form letters." See p. 13,250.

through parallel track."[18] In other words, there shouldn't be any access permitted before Phase III testing.

Fortunately, the final proposal offered that enrollment of patients in clinical trials should precede or be simultaneous with drugs offered on the parallel track. However, the proposal emphasized, "While the goal of making promising investigational agents more widely available to persons with HIV infection and no therapeutic alternatives is an important one, controlled clinical trials that yield definitive information on the safety and effectiveness of investigational new drugs must continue. This policy includes sufficient safeguards and oversight to ensure that it neither delays nor compromises the controlled clinical trials."[19]

Too many patients seeking a drug on the parallel track could interfere with clinical trials. As we shall see, the Free to Choose Medicine track would eliminate this conflict of testing approaches.

One criteria by which FDA could terminate access to medications was "[e]vidence that the parallel track study is interfering with the successful enrollment in, and completion of, adequate and well-controlled studies of this or other investigational drugs."[20]

The parallel track protocols also listed criteria for expanding access to drugs that had not passed through the full FDA approval process "to those persons with AIDS and HIV-related diseases who are without satisfactory alternative therapy and who cannot participate in the controlled clinical trials."[21]

FDA notes, "The patient cannot participate in the controlled clinical trials because: (a) The patient does not meet the entry criteria for the controlled clinical trials, or (b) The patient is too ill to participate, or (c) Participation in controlled clinical trials is likely to cause undue hardship (e.g. travel time) as defined by the protocol, or (d) The controlled clinical trials are fully enrolled."[22] As these provisions make clear, not just any patient could access drugs.

Once again, the parallel track was in an uncomfortable tension with the standard FDA track. Too many patients seeking a drug on the parallel track could interfere with clinical trials. As we shall see, the Free to Choose Medicine track would eliminate this conflict of testing approaches.

Parallel Track Criteria

Under the new protocols, sponsors wanting to get a drug on the parallel track were required

[18] *Ibid.*, p. 13,251.

[19] *Ibid.*, p. 13,256.

[20] *Ibid.,* p. 13,259.

[21] *Ibid.*, p. 13,256.

[22] *Ibid.*, p. 13,257.

to submit a request to FDA. The "FDA will refer all parallel track proposals to the AIDS Research Advisory Committee … a committee chartered by the National Institute of Allergy and Infectious Diseases."[23] The committee then made its recommendation, but the FDA had to deliver the final decision about whether a medication could be placed on the parallel track. A sponsor could ask that rather than the application going to the committee, FDA instead could consider data the sponsor submitted directly.

The protocols offered a long list of criteria upon which the FDA would judge a request that a drug be offered on the parallel track. The protocols emphasized data collection and monitoring patient experience with the test drug. Physicians treating patients were required to provide data to the drug's sponsor, and that sponsor would then be required to establish a Data and Safety Monitoring Board to evaluate the submitted information and, if serious problems arose, to recommend terminating access to the drug.

New Drug Approved

Less than six months after it was authorized, the parallel track bore fruit. On October 5, 1992, FDA granted approval of the anti-viral drug stavudine—under Bristol Myers Squibb's brand name Zerit—to be offered to patients on that track. It is estimated that some 12,000 patients received that drug on the parallel track.[24] During that period, 8,127 patients also received stavudine in traditional clinical trials. That drug received full FDA approval on December 21, 1995.[25] The parallel track cut three years off the time it would have normally taken stavudine to reach those 12,000 people suffering with AIDS/HIV.

4. Complex Paths to Expedite Drug Approval

Although successful, the parallel track was apparently only used in this single instance, for a number of reasons.

First, the existence of that track itself and the prospect it would be utilized even more, shined an even harsher light on the FDA's inefficiencies. Under pressure from Congress and advocacy groups, and not wanting to appear callously dragging its feet while thousands died, FDA undoubtedly gave priority to expediting AIDS/HIV drugs, no matter where they were in the official certification progress.

Second, the AIDS/HIV crisis spurred reforms from Congress and the executive branch. In the short run, one of those reforms, the accelerated

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[23] *Ibid.*

[24] "Parallel Track Drugs," First Clinical Research, November 29, 2005, https://firstclinical.com/fda-gcp/?show=2005/RE%20Parallel%20track%20drugs%202&format=fulllist; also see "FDA Approval of Stavudine (d4T)," *AIDS-Info*, June 27, 1994, https://aidsinfo.nih.gov/news/116/fda-approval-of-stavudine--d4t-

[25] Robert Anderson, Lisa Dunkle, *et al.*, "Design and Implementation of the Stavudine Parallel-Track Program," *The Journal of Infectious Diseases*, Volume 171, Supplement 2, "Treatment Trends in Human Immunodeficiency Virus Disease," March 1995, pp. S118–S122, https://www.jstor.org/stable/30133583?seq=1#page_scan_tab_contents

approval option (see below), helped deliver an effective drug that, along with stavudine, reduced AIDS/HIV deaths significantly. This, in turn, reduced some of the urgency to use the parallel track.

Third, the parallel track still left too much decision-making in the hands of the FDA, rather than patients, physicians, and drug developers. It was the best new option around, but it still needed to go further.

DESPITE THE SUCCESS OF PARALLEL TRACK, FDA DID NOT EXTEND THE PARALLEL TRACK OPTION TO OTHER AILMENTS. ONE REASON THIS OCCURED IS THAT THE POLITICAL PRESSURE AND ORGANIZED ADVOCACY THAT FORCED THE CREATION OF THE PARALLEL TRACK DID NOT EXIST FOR OTHER AILMENTS.

The April 15, 1992, *Federal Register* posting that announced the parallel track documented, "Many comments supported the expansion of the parallel track mechanism to other life-threatening diseases. Some comments supported immediate expansion to other diseases. Comments from individuals as well as manufacturers and professional associations expressed the view that the parallel track policy for AIDS and other HJV-related disease should serve as a pilot project to work out specific appropriate administrative procedures."[26] The desire for a swifter FDA certification process clearly went beyond the AIDS/HIV community.

Accelerated Approval

Despite the success of parallel track, FDA did not extend the parallel track option to other ailments. One reason this occurred is that the political pressure and organized advocacy that forced the creation of the parallel track did not exist for other ailments. Instead of offering the parallel track for all ailments, FDA created other paths by which it hoped drugs could be approved more quickly. In the same April 15, 1992, issue of the *Federal Register* announcing the parallel track, it sought comments for "New Drug, Antibiotic, and Biological Drug Product Regulations; Accelerated Approval."[27] This path was open to all significant new drugs, antibiotics, and biological products, not just AIDS/HIV medications. FDA argued investigatory drugs should be eligible for accelerated approval "[w]hen approval can be reliably based on evidence of the drug's effect on a surrogate endpoint that reasonably suggests clinical benefit or on evidence of the drug's effect on a clinical endpoint other than survival or irreversible morbidity, pending completion of any necessary studies to establish and define the degree of clinical benefits to patients."

In other words, if there is strong evidence that a drug would have such beneficial effects that it would help to ensure survival for patients when clinical trials are completed, there is good reason to hurry the review and approval of the

[26] *Federal Register*, Volume, 57, Issue No. 73, April 15, 1992, p. 13,250.

[27] *Federal Register*, April 15, 1992, p. 13,234.

drug so it can be marketed to patients. That rule change, which was proposed on April 15, 1992, was approved on December 11, 1992.

This FDA rule also resulted in positive outcomes. On December 6, 1995, just a few weeks before full FDA certification of stavudine, FDA approved Invirase (saquinavir), the first protease inhibitor, a mere three months after its sponsor sought accelerated approval.

DRUGS CONSIDERED CAN OFTEN BE EXPEDITED UNDER OTHER EXPEDITED PATHS AS WELL. THIS IS BECAUSE THE VARIOUS PATHS DO NOT DEAL WITH IDENTICAL STAGES OF THE CERTIFICATION PROCESS, SO A DRUG ON ONE PATH MIGHT ALSO TAKE ADVANTAGE OF ANOTHER PATH.

In the two years that followed, AIDS/HIV deaths dropped dramatically, from nearly 50,000 per year to around 20,000.[28]

Priority Review

The AIDS/HIV epidemic spurred Congress to act. Congress created a priority review process as part of the Prescription Drug User Fee Act of 1992 (PDUFA). This act was meant to expedite approval of a drug after it passes most efficacy tests. According to FDA, "An application for a drug will receive priority review designation if it is for a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness … A priority designation is intended to direct overall attention and resources to the evaluation of such applications."[29]

Under PDUFA, "FDA's goal is to take action on the marketing application within 6 months of receipt (compared with 10 months under standard review)."[30] The applicant for priority review pays the FDA an extra fee for this service. In 2017, Congress reauthorized PDUFA, which is now in its sixth iteration.[31]

Some 76 percent of drugs approved in 2018 (through early December) were under priority review.[32] Drugs considered can often be expedited under other expedited paths as well. This is because the various paths do not deal with identical stages of the certification process, so a drug on one path might also take advantage of another path. (See Figure 1.)

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[28] "HIV Surveillance --- United States, 1981—2008," *Morbidity and Mortality Weekly*, Centers for Disease Control and Prevention, June 3, 2011, https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6021a2.htm?s_cid=mm6021a2_w#Tab

[29] "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics," Food and Drug Administration, *OMB Control*, Issue No. 0910-0765, May 2014, p, 24.

[30] *Ibid.*, p. 25.

[31] "PDUFA VI: Fiscal Years 2018 – 2022," Food and Drug Administration, https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm446608.htm

[32] Khushboo Sharma, "CDER New Drugs Program: 2018 Update," FDA/CMA Summit, FDA Center for Drug Evaluation and Research, December 11, 2018, https://lifesciences.knect365.com/fda-cms/speakers/khushboo-sharma#track-a-the-new-wave-of-biosimilars-pros-and-office-of-new-drugs_cder-new-drugs-program-2018-update-at-the-fdacms

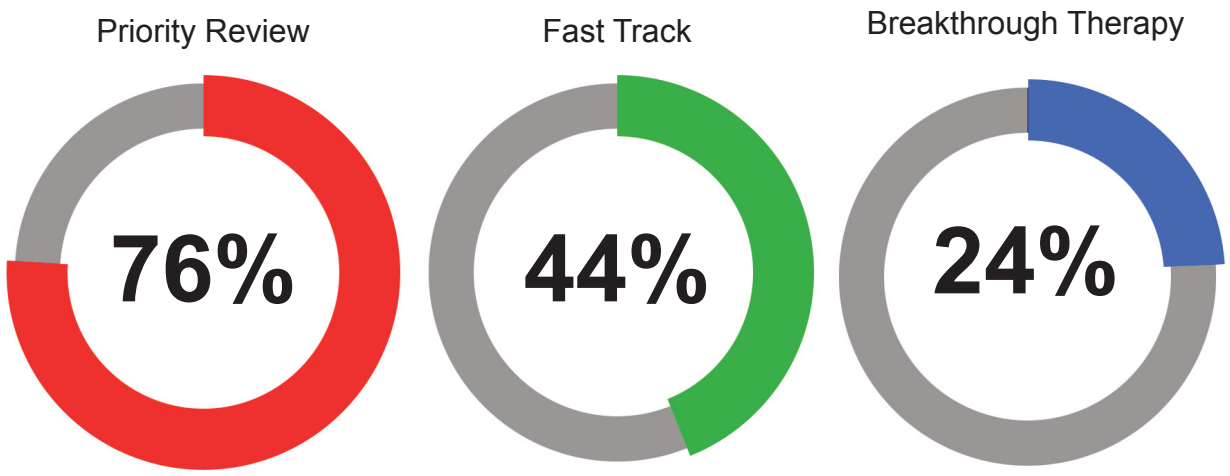
Fast Track

Congress passed the fast track path as part of the Food and Drug Administration Modernization Act of 1997. The fast track path was amended in the Food and Drug Administration Safety and Innovation Act of 2012. Under that law, FDA can approve the request of a sponsor to put a drug on this path "if it is intended … for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition."[33]

With such a designation, "There are opportunities for frequent interactions with the review team for a fast track product. These include meetings with FDA, including … end-of-phase 1 meetings, and end-of-phase 2 meetings to discuss study design, extent of safety data required to support approval, dose-response concerns, and use of biomarkers." Further, "If FDA determines, after preliminary evaluation of clinical data submitted by a sponsor, that a fast track product may be effective, the Agency may consider reviewing portions of a marketing application before the sponsor submits the complete application."[34]

Some 44 percent of drugs approved in 2018 through early December were under fast track.[35]

Figure 1. Percentage of Drugs Using Various FDA Expedited Review Options, January 2018 – Mid-December 2018*



* Note: A drug might utilize more than one option, so percentages do not add up to 100 percent.

Source: Data from presentation by Khushboo Sharma, "CDER New Drugs Program: 2018 Update," FDA/CMA Summit, FDA Center for Drug Evaluation and Research, December 11, 2018.

[33] "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics," *supra* note 29, p. 9.

[34] *Ibid.*, p. 10.

[35] Khushboo Sharma, *supra* note 32.

Breakthrough Therapy Designation

The breakthrough therapy designation was also created by the Food and Drug Administration Modernization Act of 1997. It can be applied "if the drug is intended, alone or in combination with 1 or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development."[36]

For drugs with this designation, FDA officials will be much more involved in working with the drug's sponsor to speed up the certification process. The sponsor will receive "timely advice and interactive communications to help the sponsor design and conduct a drug development program as efficiently as possible."[37] Further, "FDA intends to expedite the development and review of a breakthrough therapy by intensively involving senior managers and experienced review and regulatory health project management staff in a proactive, collaborative, cross-disciplinary review." In other words, for drugs designated as "breakthrough," FDA will be as hands-on as possible working with the sponsor to see it through to certification.

Some 24 percent of drugs approved in 2018, through early December, had received a breakthrough therapy designation.[38]

In 2018, President Donald Trump signed legislation ensuring that the FDA will not interfere with state Right to Try reforms.

Right to Try

Right to Try laws originated at the state level as a way for state lawmakers to challenge FDA delays. To date, 41 states have adopted them.[39] These laws allow terminally ill patients to access new drugs that have passed Phase I FDA safety testing but have not yet received a determination of efficacy in treating an illness. These laws do not mandate physicians report patient treatment data. In 2018, President Donald Trump signed legislation ensuring that the FDA will not interfere with state Right to Try reforms.

Compassionate Use

The expanded access option, usually referred to as "compassionate use," is a way to allow dying patients access to medications that are still in clinical trials and are only available to patients in those trials.[40] With the approval of the company producing a possibly life-saving

[36] "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics," *supra* note 34.

[37] *Ibid*., pp. 13–14.

[38] Khushboo Sharma, *supra* note 32.

[39] "Right To Try In Your State," RightToTry.org, http://righttotry.org/in-your-state

[40] "Expanded access," Food and Drug Administration, https://www.fda.gov/NewsEvents/

medication, a physician must petition FDA to access the medication and FDA must approve.

In the past, the most significant problem with the compassionate use option has been the time-consuming paperwork burden placed on physicians requesting access for their patients. In the past two years, FDA has managed to mildly reduce that burden, but gaining access is still not an easy task.

FDA heralds the fact that in recent years it has approved more than 99 percent of compassionate use requests.[41] However, this number does not take into account of those who do not submit applications because they consider the application process too burdensome or who believe there's a good chance they do not meet the criteria for such access. A patient who might have had a good opportunity to be cured by early access to a medication can be forced to wait until their illness has progressed to a critical stage, when the medication might be less likely to be effective, before they can access it.

Ad Hoc Paths

A sponsor of a new drug might rightly look at these options and ask, "Which one should I seek?" Indeed, sponsors of new medications seeking FDA approval can require the services of consultants to help make these choices and sort through and guide the sponsor through all the available options. Therein lies the problem with these approaches. FDA might argue several options to expedite drug approval already exist and, therefore, that significant structural reform is not needed. But the complexity and details of the various paths show this claim to be problematic. FDA ultimately decides which promising medications can be considered and on which expedited paths.

While FDA might mean well, substantive reform is needed. There must be a better way, and, thankfully, there is: Free to Choose Medicine.

These certification options do not approach the openness and straightforward simplicity underlying the parallel track option, which was also far from perfect. Parallel track contained too many restrictions that discouraged future users, which explains, in part, why there was no major push to offer the parallel track option for serious illnesses other than AIDS/HIV.

There's no question the current model is in need of substantial reform. A Tufts survey found, despite FDA's many alternative tracks, it takes on average more than a decade to bring a new product from the research lab to market, at an average cost of $2.6 billion.[42] While FDA might mean well, substantive reform is needed. There must be a better way, and, thankfully, there is: Free to Choose Medicine (FTCM).

PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm

[41] Michael Mezher, "FDA Approved Nearly All Expanded Access Requests in FY2016," *Regulatory Focus*, March 20, 2017, https://www.raps.org/regulatory-focus%E2%84%A2/news-articles/2017/3/fda-approved-nearly-all-expanded-access-requests-in-fy2016

[42] Tufts Center, *supra* note 1.

5. The Free to Choose Medicine Solution

Today, many ailments—for example, Alzheimer's—cause debilitation, suffering, and even death in a manner similar to what AIDS/HIV patients faced in the past. Each year, nearly 100,000 Americans die from Alzheimer's, usually after years of heavy burdens placed on family and friends who care for their loved ones. By comparison, deaths among Americans from AIDS/HIV is now less than 16,000.[43]

Unlike AIDS/HIV cases, which have been declining, Alzheimer's cases increased by 123 percent from 2000 to 2015.[44] About five million Americans suffer from Alzheimer's, compared to about 1.1 million suffering from AIDS/HIV.[45] The number of Alzheimer's sufferers is predicted to rise to more than seven million by 2025, 8.4 million by 2030, and 16 million by 2050. One estimate put the cost on the U.S. economy of Alzheimer's at $259 billion in 2017.[46]

The parallel track option created in 1992 for AIDS/HIV medications points the way toward the best option for allowing patients speedy access to safe and promising drugs—not only for Alzheimer's, but for dozens of other illnesses as well. The Free to Choose Medicine plan would create a second, more dynamic track for testing and approval of all potential new drugs.

Under FTCM, after a new drug passes the FDA Phase I safety tests and at least one round of Phase II efficacy testing, a drug manufacturer would be permitted to choose to proceed on the Free to Choose Medicine track.

FTCM would provide a number of improvements over the parallel track. First, FTCM would allow manufacturers and drug sponsors, rather than FDA, to decide whether to offer a drug through the FTCM track.

FTCM would provide a number of improvements over the parallel track. First, FTCM would allow manufacturers and drug sponsors, rather than FDA, to decide whether to offer a drug through the FTCM track. A FTCM committee would ensure that the drug has successfully passed the Phase I safety tests and one Phase II trial. After the drug passes a Phase II trial, it could be offered on the FTCM track.

Second, under FTCM, FDA would not determine which patients can access a medicine. Instead, in consultation with a physician and a drug manufacturer, the educated patient would make that choice.

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[43] U.S. Statistics Fast Facts, HIV.org. https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics

[44] "2018 Alzheimer's Disease Facts and Figures," Alzheimer's Association, 2018, https://www.alz.org/media/HomeOffice/Facts%20and%20Figures/facts-and-figures.pdf

[45] U.S. Statistics, note 43.

[46] "2017 Alzheimer's Statistics," Alzheimers.net, accessed February 10, 2019, https://www.alzheimers.net/resources/alzheimers-statistics

Third, and key to the reform, FTCM would alleviate the tension seen in the parallel track path between FDA's strong desire to mandate clinical trials and patients' need for access to medications outside of those trials, in part by creating a Tradeoff Evaluation Drug Database (TEDD).

FDA and drug manufacturers are concerned that the more individuals are permitted to access drugs outside traditional clinical trials during the test period, the fewer patients might be available for latter trials. They might also raise questions about the usefulness of information about a drug's efficacy they will garner from the FTCM track compared to the traditional track. Under FTCM, the characteristics and medical history of the patients and their experiences with the new drug treatment would be entered into TEDD, with patient privacy protected. Researchers, physicians, pharmaceutical companies, and patients would have access to this real-world data, which would highlight the effectiveness and potential problems with medications. A limited, real-world example of such testing and information gathering could be seen during the AIDS/HIV epidemic. Sufferers often smuggled and exchanged drugs not certified by FDA and shared through their informal networks experiences about which drugs worked best.

Like parallel track for AIDS/HIV, FTCM would not need congressional approval. It could be created by a regulatory change, which would start with a post in the *Federal Register*.

The parallel track for AIDS/HIV medications was created before the internet was available to the public. Access to data was more difficult then. Today, a TEDD database would be immediately and easily accessible for those wishing to collect information on medications, just like *Yelp* is for an endless array of consumer goods and services.

Under FTCM, FDA would still ultimately have to approve a new drug, but a drug's sponsor could choose the best way to demonstrate a drug's effectiveness. The TEDD database could complement clinical trials and other methods. Indeed, FTCM would not only create incentives for researchers and manufacturers to develop effective drugs, it would create incentives for them to develop innovative ways to demonstrate efficacy. As medicine and therapies move from traditional drugs (mixtures of chemicals) to biologics, which involve biological materials, and genetically engineered cures, different ways of demonstrating safety and efficacy will undoubtedly be needed. FTCM and TEDD would facilitate and focus energy on such innovation, rather than on maneuvering through the FDA's burdensome and costly procedures.

6. The Path to FTCM

Like parallel track for AIDS/HIV, FTCM would not need congressional approval. It could be created by a regulatory change, beginning with a post in the *Federal Register*. Once comments have been received, FDA could implement the FTCM model without any new legislation from Congress.

The Trump administration could also initiate smaller steps that would move the country toward FTCM. One example is the creation of a pilot TEDD program.

Although congressional action is not required, Congress could enact FTCM in legislation. In the years following the creation of the parallel track, Congress did enact other reforms of FDA to speed up the drug certification process. Congress could also raise consciousness about the FTCM option through hearings and other activities, the way Rep. Waxman did to promote FDA reform to facilitate quicker access to AIDS/HIV medications.

All these options begin with support from patient groups, researchers, manufacturers, and members of the public who desire to make medications and therapies available in a timely manner to those suffering with ailments. For the necessary, far-reaching reforms called for in this paper to be enacted, there must be a sense of urgency among the public, just as there was when popular opinion sparked the reforms of the 1990s.

Conclusion

FTCM is a true solution to the FDA certification bottleneck, taking the parallel track model that was developed to give AIDS/HIV sufferers in the 1990s access to much-needed treatments to its logical conclusion. And it's not merely a theoretical policy proposal. An alternative version of FTCM was adopted by Japan to govern its regenerative medicine products.[47] Similar reforms are being adopted in China.

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With the global market for research and product development growing, U.S. pharmaceutical companies will see greater opportunities to work in partnership with foreign affiliates to bring new products to market through the approval process in Japan, and perhaps, eventually, in China. This should be an added incentive to adopt FTCM in America, because failing to adopt a similar plan would encourage innovations in this important industry to occur overseas.

However, the most important incentive for the passage of FTCM remains the need to create a system that can ensure not only the safety and efficacy of new medicines and treatments, but also ensure millions of people suffering with ailments in this country will gain access to these treatments faster than ever before.

FTCM is a clearer, streamlined system that will give companies, especially smaller ones that often cannot bear the time and costs it takes to navigate the

[47] Edward Hudgins, "Free to Choose Medicine in Japan: A Model for America," *Policy Brief*, The Heartland Institute, June 2018, https://www.heartland.org/_template-assets/documents/publications/61418_JapanFTCM1.pdf

current system, the opportunity to invest more of their resources into discovering treatments for diseases, rather than navigating the federal government's extensive bureaucracies.

The promise of fundamental reform was seen in the parallel track option nearly three decades ago. FTCM is a reform that is past due. Its time is now.

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About the Author

Edward Hudgins, Ph.D., is the research director of The Heartland Institute.

In conjunction with other department directors, Hudgins sets the organization's research agenda and priorities; works with in-house and outside scholars to produce *Policy Studies*, *Policy Briefs*, and books; contributes his own research; and works with Heartland staff to promote Heartland's work.

Before joining Heartland, Hudgins was the director of advocacy and a senior scholar at The Atlas Society, which promotes the philosophy of reason, freedom, and individualism developed by Ayn Rand in works such as *Atlas Shrugged*. His latest Atlas Society book was *The Republican Party's Civil War: Will Freedom Win?*

While at The Atlas Society, Hudgins developed a "Human Achievement" project to promote the synergy between the values and optimism of entrepreneurial achievers working on exponential technologies and the values of friends of freedom.

Prior to this, Hudgins was the director of regulatory studies and editor of *Regulation* magazine at the Cato Institute and a senior economist at the Joint Economic Committee of the U.S. Congress, specializing in trade and regulatory issues.

Hudgins also worked at The Heritage Foundation as deputy director for domestic policy studies and as the director of the Center for International Economic Growth, where he pioneered the concept of an Index of Economic Freedom.

Hudgins has appeared on numerous major TV networks, including CSPAN, Fox News, MSNBC, The History Channel, and CNN, and his op-eds have been featured in papers like the *Washington Times*, *Wall Street Journal*, *Boston Globe*, and *Philadelphia Inquirer*.

Hudgins earned a bachelor's degree in government from the University of Maryland, a master's degree in political theory from American University, and a Ph.D. in political philosophy and international political economy from the Catholic University of America. He has taught at universities in Germany and the United States.

About The Heartland Institute

Founded in 1984, The Heartland Institute is an independent national nonprofit research organization. It is a tax-exempt charity under Section 501(c)(3).

The mission of The Heartland Institute is to discover, develop, and promote free-market solutions to social and economic problems. Three things make Heartland unique among free-market think tanks:

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- We produce four monthly public policy newspapers – *Budget & Tax News*, *Environment & Climate News*, *Health Care News*, and *School Reform News* – which present free-market ideas as news rather than research or opinion.

- We promote the work of other free-market think tanks on our websites, in our newspapers, at our events, and through our extensive government and media relations. No other institution does more to promote the work of other think tanks than we do.

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For more information, please visit our website at www.heartland.org or call 312-377-4000.