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NOMINATION OF DR. ROBERT CALIFF TO BE COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEARING

OF THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS

UNITED STATES SENATE

ONE HUNDRED SEVENTEENTH CONGRESS

FIRST SESSION

ON

EXAMINING THE NOMINATION OF ROBERT MCKINNON CALIFF, OF NORTH CAROLINA, TO BE COMMISSIONER OF FOOD AND DRUGS, DEPARTMENT OF HEALTH AND HUMAN SERVICES

DECEMBER 14, 2021

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C O N T E N T S

STATEMENTS

TUESDAY, DECEMBER 14, 2021

NOMINATION OF DR. ROBERT CALIFF TO BE COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Tuesday, December 14, 2021

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The Committee met, pursuant to notice, at 10:01 a.m., in room G50, Dirksen Senate Office Building, Hon. Patty Murray, Chair of the Committee, presiding.

Present: Senators Murray [presiding], Sanders, Casey, Baldwin, Murphy, Kaine, Hassan, Smith, Rosen, Lujan, Hickenlooper, Burr, Collins, Cassidy, Braun, Marshall, Scott, Romney, and Tuberville.

OPENING STATEMENT OF SENATOR MURRAY

The CHAIR. Good morning. This Committee will come to order. The Senate Health, Education, Labor, and Pensions Committee will please come to order. Today we are holding a hearing on the nomination of Dr. Robert Califf to serve as Commissioner of the Food and Drug Administration. Ranking Member Burr and I will each have an opening statement, then Senator Burr will introduce the nominee.

After Dr. Califf's testimony, Senators will have 5 minutes for a round of questions. And while we were again unable to have this hearing fully opened to the public or media for in-person attendance, live video is available on our Committee website at *help.senate.gov*. And if you are in need of accommodations, including closed captioning, you can reach out to the Committee or to the Office of Congressional Accessibility Services.

We received Dr. Califf's formal nomination on November 15th, his Office of Government Ethics paperwork on November 17th, and his Committee paperwork on November 22nd. Dr. Califf, thank you for joining us. You are a long ways away there, but we can see you.

Dr. CALIFF. I think I can see you there, thank you.

[Laughter.]

The CHAIR. I want to welcome your family who is with you today, your wife, Lydia, your son Sam, your daughter Sharon, your son in law, Chris, and your grandchildren, Brooke and Noah as well. Welcome to all of you. Families across the country count on the Food and Drug Administration every day to follow the science and the

data and keep them safe, and COVID–19 has put that rule in the spotlight like never before. This pandemic has been incredibly hard on our Nation. It has killed over 800,000 Americans and upended our lives in countless ways.

As we continue our work to end this crisis and rebuild our Nation stronger and fairer, we are all grateful for the tireless work of FDA scientists to review and authorize safe and effective tests, treatments, and of course, vaccines for COVID–19.

While the COVID–19 pandemic remains one of the most urgent challenges in our Nation, there are countless other ways FDA works—that work matters to families. Every day people put the well-being of themselves, their families, and even their pets in FDA's hands. When we sit down for a meal, we count on FDA's efforts to ensure the safety of our food supply and provide us with the information we need to make healthy choices.

When we get our prescriptions filled or rely on medical devices to stay healthy, we count on FDA's work to uphold the gold standard of safety and effectiveness. The FDA needs strong leadership to continue that work and to address other pressing challenges—challenges like the opioid crisis. We lost over 100,000 people to drug overdoses between April 2020 and April 2021. That is an all-time high and nearly double the number of deaths we saw only 5 years ago. Challenges like youth tobacco use. E-cigarettes and other flavored tobacco products have led to skyrocketing tobacco use among kids.

According to the CDC, 2 million youth use e-cigarettes and a quarter of that group uses them daily. Challenges like antimicrobial resistance, a threat which could make current treatments for infections fundamentally ineffective, and common procedures like joint replacements or organ transplants and C-sections life threatening. Challenges like improving health equity. We know too many communities are left behind in our public health response, including in clinical trials, which historically have left out certain populations like people who are pregnant, people of color, and others.

This undermines people's health by delaying information they and their health care providers need to understand how a treatment will affect them specifically or whether it is safe during pregnancy, and by making it hard to identify differences in the safety and efficacy of treatments for these patient populations. So over the last few years, I have repeatedly raised the need for FDA to improve diversity in clinical trials. Then there is the constant challenge of keeping pace with discovery. Senator Burr and I both are focused on making sure FDA stays ahead of the massive discoveries and technological advances being made in medical science and biotechnology.

While we need a strong leader at FDA to tackle all of these challenges, we also need to make sure we are giving the agency the tools it needs to do this work and keep our families safe. That is why in the year ahead, this Committee is continuing its long tradition of working in a bipartisan way to reauthorize all the user fee programs set to expire in 2022. The user fee programs are critical to supporting the agency's work to review and approve products

and uphold the gold standard of safety and effectiveness in a timely and efficient manner.

Without these programs, it would take longer for FDA to help bring safe and effective medical devices to the U.S. market and to review generic and biosimilar drugs, which can lower drug costs by offering patients cheaper alternatives for drugs they need. And as we work to support FDA's drug review process, we also need to stop drug companies from misusing the process to keep cheaper drugs off the market.

Patients desperately need us to fight skyrocketing drug costs with every tool in our arsenal, and that includes making sure affordable drugs are not kept off the shelf by pharmaceutical companies who are gaming the FDA approval system. We also need to make sure the Food and Drug Administration has the authority it needs to keep families safe from products that have gone for too long with too little scrutiny. When it comes to cosmetics, we have discovered known carcinogens like asbestos and formaldehyde in products like baby powder, children's makeup kits, and hair products.

When it comes to dietary supplements, people across the country who are looking to make healthy choices are faced with a shelf full of products that make claims about their health benefits but lack rigorous oversight because FDA does not have the authority to collect basic information about those products or even to know what products are on the market. Families across the country buy and use these items every day. They deserve to know all the products they entrust their health to are subject to type of careful FDA oversight they already trust to keep their food and drugs and medical devices safe.

Families also deserve to know they have an experienced leader at the FDA who understands the many challenges our Nation is facing and the importance of ensuring science comes first. Dr. Califf has worked on these issues before, when he was previously confirmed to lead FDA in an overwhelmingly bipartisan vote. I look forward to working with him again to ensure FDA continues to protect families across the country, uphold the gold standard of safety and effectiveness, and put science and data first.

Throughout this crisis, FDA has empowered its experts and ensured its decisions are based in science and data. And as we have seen him in the growth of misinformation around issues like vaccines and reproductive health care, maintaining that commitment to always put science first will be more important than ever to maintaining the trust of the American people.

Now, before I turn it over to Ranking Member Burr for his opening remarks, I seek unanimous consent to put in the record 13 letters in support of Dr. Califf's nomination signed by more than 90 organizations representing health care providers, academic research, and patient advocates, including a letter from six former FDA Commissioners appointed by Presidents of both parties. So ordered.

[The following information can be found on page 42 in Additional Material:]

The CHAIR. I will turn it over to Ranking Member for your opening remarks and for introducing Dr. Califf.

OPENING STATEMENT OF SENATOR BURR

Senator BURR. Thank you, Madam Chair. Thank you for holding this important hearing today. With the indulgence of the Chair, I am going to include Dr. Califf's introduction in my opening statement before the Committee. Dr. Califf, last time you were here interviewing for this job, I introduced you to my colleagues as a wonderful father, grandfather, great doctor, great man. Let me say to my colleagues, all that remains the same today. Welcome back. Dr. Califf is a distinguished North Carolinian who previously served as Commissioner of the Food and Drug Administration under President Obama from February 2016 until January 2017.

Prior to becoming Commissioner, Dr. Califf served as the Deputy Commissioner of the FDA's Office of Medical Products and Tobacco beginning in February 2015. Before joining the FDA, Dr. Califf was a Professor of Medicine and Vice Chancellor for Clinical and Translational Research at Duke University in Durham, North Carolina. Dr. Califf spent more than 35 years in leadership roles at his alma mater, including the positions of Director of Translational Medicine Institute and the Director of Clinical Research Institute. He has also worked to move the promising field of translational science forward as the director of the Clinical Trials Transformation Initiative.

Dr. Califf currently is the head of Clinical Policy and Strategy for Verified Life Science and Google Health at Alphabet, Google's parent company. His experience also includes serving as vice Chancellor for Health Data Science and Director of Duke Forge and the Donald F. Fortin, M.D. Professor of Cardiology at the Duke University School of Medicine. Dr. Califf's unique perspective as an FDA Commissioner, coupled with his understanding of partnerships with the private sector and academia that assist in fueling innovation will be vital if confirmed as the next FDA Commissioner.

Dr. Califf, thank you for being here to answer questions today. I say to my colleagues, I am not sure you could write a resume of somebody more qualified to be considered for Commissioner of the FDA than Rob Calif. To your family, you should be proud today. All of the criticism he will endure during this process is the result of his own success. Thank you for the sacrifice that you are making to allow him to return to the FDA. I am thankful to finally have an opportunity to hold a hearing on one of the most significant positions in the Administration during the worst pandemic in over a century.

This Administration has left the FDA Commissioner position open since January 20th, almost a full year in the middle of a pandemic. I am disappointed that it took so long, but I am glad to see you here again sitting before this Committee. Since your last—since you were last here, the FDA has made some major strides in updating and modernizing their behavior.

Now, in the midst of a global response to the pandemic, so much more is at stake. The FDA is responsible for ensuring the safety and effectiveness of medical devices, medical products in the United States and protecting our Nation's food supply.

Safety and efficacy is your mission. Is the product safe for use and does it work as intended? FDA regulates approximately $0.20

of every dollar in the U.S. economy. The products and practices it regulates are diverse, and there will be more demands on your time than there are hours in a day.

You are familiar with the FDA as an agency and with its responsibilities, its challenges, and its ability to reach the lives of every American. Because of FDA's reach, there are infinite things that you could do if you are confirmed, but your priorities should align with where FDA can have the greatest impact, supporting the next generation of biomedical science and innovation, and protecting our Country from public health threats. It has been almost 5 years since you last served at the FDA.

You will be a newcomer to the agency's pandemic response and to the ways the FDA has improved over the past 2 years. You are filling the shoes of a legend. The Nation has been fortunate to have Janet Woodcock at the helm. The FDA success is her success, and we need to build on that. I have significant concerns that FDA could revert to its old ways of doing things, going back to the ways before COVID.

Your last—you last led the agency during peacetime. We need a wartime Commissioner who will lead us through the next phase of the response to coronavirus, and build a stronger, more nimble FDA for patients and America's consumers. The past 2 years have tested the FDA. Its authorities and regulatory practices have come under scrutiny as the gatekeeper for medical countermeasures needed to protect us against coronavirus. The pandemic has exacerbated existing systemic challenges at the agency and created entirely new ones that you will face if confirmed.

The FDA has made historic progress. The agency finally leaned into its authorities to move as quickly and safely as possible. It worked with manufacturers to develop and rapidly scale up manufacturing of 3 vaccines, 12 treatments, and more than 420 tests to protect us against, detect, and diagnose a virus. Many of these countermeasures were developed and authorized for use in a matter of months or even weeks, without compromising safety and efficacy, a testament to the agency and its partnership with innovators. FDA provided flexibility and certainty. It made all the difference. The next Commissioner cannot take their foot off the gas. The agency has come too far.

The FDA's regulatory readiness is important for the next threat that we will face, but also for the unmet needs for devastating diagnosis like cancer, Alzheimer's, and ALS. The pandemic demonstrated that medical products can be developed more quickly without compromising the FDA's gold standard. The time it takes to develop a new drug increased from an average of 7 years in 1997 to 9 years in 2017.

According to NIH, it can take up to 7 years to develop a diagnostic. We need to go the other way. We developed treatments and vaccines for COVID in under a year and diagnostic test in a matter of a few months. Many vaccines and treatments used during COVID leveraged platform technology that we can adapt to address new targets. I think they are one of the best ways to accelerate development at the FDA is to work with innovators to streamline the development and review of new products built on these cutting-

edge platforms, whether for new pathogen or for a lifesaving, life changing disease.

Next year, this Committee will be charged with evaluating the FDA's user fee program and consider their reauthorization. I have strong, deeply held feelings about this important program. I have served in Congress for all but the first user fee process. Since their creation, user fee programs have grown to enormous sizes. Over the decades, the PDUFA program fees collected have roughly doubled, and MDUFA program fees have more than quadrupled. This growth in user fees from industry weakens FDA's accountability to Congress and to patients that we serve.

The purpose of the user fee program is to supplement the money FDA received from Congress for the review of medical products to bring treatments and therapies to the American people as quickly as possible. Today, after all, the agencies have been through, with what they have been through with the pandemic response, our approach to the user fees will undoubtedly, undoubtedly look different.

Today, after all the—as FDA and industry work to finalize the commitment letters for Congress to review next year, I expect that each agreement will take stock of lessons learned over the last 2 years. Dr. Califf, should you be confirmed, I look forward to working with you during the most important user fee cycle that this Committee has faced. I spent almost 30 years working to hold the FDA accountable so that the American—Americans benefit from innovative medicines.

The best way for the agency to achieve this goal is to provide clear, predictable pathways for markets—for products to come to market. FDA has made progress on this for some of the products it regulates, approving lifesaving drugs and medical devices every year.

FDA has issued specific guidance for rare disease, cell and gene therapy, and complex generic drugs, but more work remains to speed the slow gears of regulation. FDA also still has much to do to provide a clear and predictable pathway to market for tobacco products and diagnostic tests. Leadership, vision, and understanding of the innovation of products are critical to fair, predictable regulatory pathways for any product regulated by the FDA.

The Centers for Tobacco Products receives the second highest user fee dollars of any center at the agency, except for the drug center. More than a decade after receiving authority from Congress, FDA just recently issued the foundational rules to provide a regulatory roadmap for a new and potentially less harmful tobacco product.

Can you imagine if FDA did not have foundational regulations for the review of new drugs while still requiring products to submit applications? Despite 13 years and more than $7.5 billion, it has authorized under the premarket pathway only one, one, Vapor product, a class of product that can provide a new, potentially less harmful alternative for lifelong smokers.

CTP is charged with the regulation of tobacco products, which includes a mission to regulate these products for the protection of public health. It is not meeting that mission, either. According to data FDA gave me in 2019, CTP spent millions more on advertise-

ments than it did on enforcement against bad actors. Dr. Califf, should you be confirmed, I would ask you to take a hard look at the Tobacco Center and get the house in order. Enormous innovation is occurring in areas of diagnostic tests. We have experienced this innovation throughout the pandemic response.

The laboratory community rapidly developed tests to detect, diagnose, and surveil the coronavirus. There was confusion early on in the response as to whether these tests were under FDA's regulatory purview, and if so, what was required of them to be available to the American people.

Public health officials, test developers, providers, and patients need the law to provide regulatory certainty and predictability that allows for innovation to continue on the same trajectory we are experiencing during the pandemic.

Dr. Califf, I hope you can agree that Congress needs to speak to resolve this decades old issue once and for all. If you are confirmed as Commissioner, which I expect you will be, you will be responsible for maintaining FDA's mission as we enter a new era of biomedical innovation. This new era rule will require FDA to recruit, higher, and retain the right talent. FDA has long faced systemic hiring challenges. It will be on—it will be one of the top challenges that you face as a Commissioner.

If you are confirmed, I look forward to working with you to help to address this issue. You will be responsible for policy decisions to help Americans as they safely return to normal life, to prepare to respond to future pandemics, and to build upon successful policies that have enabled medical innovation to reach patients more quickly. Effective and accountable leadership at FDA is paramount.

My questions today are intended to make sure that you are up to the task of leading the FDA while we are still battling a once in a lifetime pandemic. I urge you to focus on what matters most, to not lose sight of all the ground gained, and to use the tools we have given you to your fullest extent. I look forward to our conversation today and hearing your plans for returning to the agency to address many challenges that we face. With that, Madam Chair, I yield the floor.

The CHAIR. Thank you, Senator Burr. We will turn it over to Dr. Califf for his opening remarks. Again, welcome to our Committee, and welcome to your family as well.

STATEMENT OF HON. ROBERT CALIFF, M.D., DURHAM, NORTH CAROLINA

Dr. CALIFF. Thank you so much, Chair Murray and Ranking Member Burr. I want to thank you and Members of the Committee for inviting me here today to discuss my nomination to be Commissioner of the Food and Drug Administration.

Five years ago, I was before you in the same position. Much has happened over those 5 years, including the devastating COVID–19 pandemic, but many fundamental issues I addressed at that time remain important areas for the FDA, our Country, and the world to advance toward an era of unprecedented health.

I am excited to be accompanied by my family today and thank you for your kind introductions of them. Also want to take a mo-

ment to honor my parents who were with me at the last meeting and who passed away peacefully in their 90's.

The support of my family has been essential to my career. This unique opportunity to help create a better world for my grandchildren is personally motivating. I previously served with pride as FDA Commissioner, and I am honored that President Biden has nominated me to lead the FDA for a second time.

I want to thank Dr. Janet Woodcock, the rest of the FDA leadership team, and the entirety of the FDA workforce for their exemplary service over the years, and especially during the COVID–19 pandemic. To the many Committee Members I have met with over the last several weeks, about 23 total, including Committee Members, I thank you all for your willingness to share with me your perspective on ways the FDA can better serve the American people.

If confirmed, I will be a Commissioner who understands the importance of working closely with Congress, as well as other parts of the executive branch. I will also be a Commissioner who can hit the ground running because of my past experience as a civil servant and in leading the agency.

My career has been dedicated to advancing the health of individuals and the public as a physician, researcher, and leader in both the public and private sectors, as well as academia. My family, like many American families, has experienced firsthand how important it is to find a critical balance between appropriate safeguards for patients and innovative treatments.

My daughter was born with a serious congenital heart defect requiring open heart surgery as an infant. My mom benefited directly from the accelerated approval of new drugs from multiple myeloma that without a doubt and in meaningful years to her life. My professional experiences too have shaped my understanding of our health system over the years.

As a physician, I care for people with serious cardiovascular disease, and I worked with colleagues on the development and evaluation of life saving medicines and technologies for the treatment of heart disease that have helped millions of Americans.

This experience also taught me about the painstaking work of developing a safe and effective medical product, then conducting the critical clinical trials and seeking FDA approval for that product. In this process, the majority of proposed new drugs and devices failed because the risks outweigh the benefits. I learned firsthand that it is essential that we produce high quality evidence to sort the effective and effective treatments.

My first priority, if confirmed, will be emergency preparedness and response. The FDA must continue to be a strong partner in battling COVID–19, taking into account lessons learned from the pandemic so we can apply them to the ongoing current pandemic and so we are ready for the next one.

Second, all FDA's actions regarding the products of the agency, that the agency regulates, must focus on protecting consumers and patients. Safety matters. Now is the time to develop a systematic approach to evidence generation that will improve patient safety and provide a much more efficient way to understand the benefits and risks of medical products when used in practice, and to ensure

that our food is safe. And we must protect kids from tobacco products.

As surveys indicate, youth use remains at an alarming rate. Our Nation is also experiencing an epidemic of addiction and overdose, with over 100,000 overdose deaths recorded over a 12 month period for the first time ever. FDA must work with the public health, clinical, and policy committees to turn the tide.

Third, FDA must stay current on the latest advances in science and technology in order to provide guidance to industry and stakeholders on everything from clinical trial conduct to regenerative medicine to best practices for protecting the safety of the U.S. food supply.

With each of these priorities, a common thread is my commitment to ensuring that the agency is more inclusive, diverse, equitable, and accessible in the work it does for the American public.

As I work to implement these priorities, attracting and retaining FDA scientific workforce maybe even more important than any particular policy because it is the agency's day to day decision-making that protects the public.

This is a once in a generation time for public health, and the FDA must continue to play a vital role in protecting and promoting the health of all Americans by leveraging the acceleration of technology and biomedical knowledge.

If confirmed, I would be honored to lead the agency again. Thank you for allowing me to testify before you today, and I am happy to take your questions.

[The prepared statement of Dr. Califf follows:]

PREPARED STATEMENT OF ROBERT M. CALIFF

INTRODUCTION

Chair Murray and Ranking Member Burr, I want to thank you and Members of the Committee for inviting me here today to discuss my nomination to be Commissioner of the Food and Drug Administration (FDA). Five years ago, I was before you in the same position. Much has happened over those 5 years, including the devastating COVID–19 pandemic, but many fundamental issues I addressed at that time remain important areas for the FDA, our country and the world to advance toward an era of unprecedented health.

I am excited to be accompanied by family today. Sitting behind me are my wife of 48 years and high school sweetheart, Lydia; two of our three children, Sharon and Sam; and two of our six grandchildren, Brooke and Noah. I also want to take a moment to honor my parents, who were with me at the last hearing, and who passed away peacefully in their 90's. The support of my family has been essential to my career. The unique opportunity to help create a better world for my grandchildren is personally motivating.

I previously served with pride as FDA Commissioner, and I am honored that President Biden has nominated me to lead the FDA for a second time. I also want to thank Dr. Janet Woodcock, the rest of the FDA leadership team, and the entirety of the FDA workforce for their exemplary service over the years and especially during the COVID–19 pandemic.

To the many Committee Members I have met with over the last several weeks: I thank you all for your willingness to share with me your perspectives on ways the FDA can better serve the American people. If confirmed, I will be a Commissioner who understands the importance of working closely with Congress, as well as other parts of the executive branch. I will also be a Commissioner who can hit the ground running because of my past experience as a civil servant and in leading the Agency.

BACKGROUND

My four-decade career has been dedicated to advancing the health of individuals and the public as a physician, researcher, and leader in both the public and private sector—as well as academia. But, like each of you, my understanding of our health system was shaped by both my personal and professional life experiences, which will guide my work at the FDA, if confirmed.

Personal

My family, like many American families, has experienced firsthand how important it is to find a critical balance between appropriate safeguards for patients and innovative treatments.

My daughter was born with a serious congenital heart defect requiring open heart surgery as an infant. My mom benefited directly from the accelerated approval of new drugs for multiple myeloma that, without a doubt, added meaningful years to her life.

Professional

My professional experiences, too, have shaped my understanding of our health system over the years. When I began my career as a cardiologist, heart attack was the leading cause of death in the United States and our understanding of the cause of heart attack was limited. I, along with a global network of health professionals, worked to figure out why. Together we developed "clot busting" drugs to restore blood flow to the heart, improve the recovery of the heart muscle and help prevent future heart attacks. We also developed life-saving technologies, including balloon angioplasty, cardiovascular stents, and implantable defibrillators, that have helped millions of Americans; and we stopped the development of numerous drugs and devices for which the risks outweighed the benefits. Thanks to these technologies death rates from acute heart problems have been cut in half.

This experience also taught me about the painstaking work of developing a safe and effective medical product, then conducting the critical clinical trials and seeking FDA approval for that product. Like clinical decisions, FDA decisions are best made when the evidence is robust. My career has been focused on developing better systems for generating reliable evidence to support the everyday decisions that consumers, patients, clinicians and policy makers must make to achieve better health.

PRIORITIES

My priorities, if confirmed, would be: emergency preparedness and response; consumer and patient protection; and modernization and innovation.

When it comes to emergency preparedness and response, the FDA must continue to be a strong partner in battling COVID–19. And, it must have infrastructure in place that reflects lessons learned from this pandemic so it is ready for the next one.

Second, all FDA's actions regarding the products the agency regulates must focus on protecting consumers and patients. Safety matters. Now is the time to develop a systematic approach to evidence generation that will improve patient safety and provide a much more efficient way to understand the benefits and risks of medical products when used in practice. The FDA must continue to build the science base needed to give people confidence that their food is safe and their medical products are safe and effective. And we must protect kids from tobacco products, as surveys indicate youth use remains at an alarming rate.

Our Nation is also experiencing an epidemic of addiction and overdose, with over 100,000 overdose deaths recorded over a 12-month period for the first time ever. FDA must work with the public health, clinical and policy communities to turn the tide.

Third, FDA must stay current on the latest advances in science and technology in order to provide guidance to industry and stakeholders on everything from clinical trial development to best practices for protecting the safety of the U.S. food supply.

With each of these priorities, a common thread is my committment to ensuring that the agency is more inclusive, diverse, equitable and accessible in the work it does for the American public.

As I work to implement these priorities, I would also continue my previous focus on investing in our workforce. Attracting and retaining the FDA's scientific workforce may be more important than any particular policy because it is the agency's day-to-day decision-making that protects the public. The scientific and technical world is moving quickly—the FDA needs the talent to keep up and protect the public while supporting scientific innovation.

CONCLUSION

This is a once-in-a-generation time for public health, and the FDA must continue to play a vital role in protecting and promoting the health of all Americans by leveraging the acceleration in technology and biomedical knowledge. If confirmed, I would be honored to lead the agency again. Thank you for allowing me to testify before you today, and I am happy to take your questions.

The CHAIR. Thank you very much, Dr. Califf. We will now begin a round of 5 minute questions, and I ask my colleagues, please keep track of your clock and stay within your 5 minutes. Dr. Califf, let me begin. The opioid use epidemic continues to cause tremendous harm to far too many families and communities.

As I mentioned in my opening statement, the new CDC data shows that more than 100,000 people died of drug overdose in the 12 months ending in April 2021. That is a new and very grim record high. During your time as FDA Commissioner, you started the process of reevaluating how the agency approached the approvals of opioid. What are the actions the FDA can take to address this worsening crisis?

Dr. CALIFF. Senator Murray, I really appreciate your bringing this up right at the start because the opioid crisis and the addiction crisis overall, now with synthetic opioids and stimulants on the streets of America, it is gut wrenching for American families.

I think all of us know someone who has been affected by it. I have had relatives in the last year who have been prescribed 30 days of opioids for minor surgery, for example, so I know we have work to do. I am happy to go over my history and working on this problem since 1999.

But you asked about what we need to do now, and I think we need to learn from all that has happened over the last several decades with this and reassess where we are today, because whatever we have done up until now is not enough. It is going to take all hands on deck, and specifically, the FDA needs to redouble its efforts on prescriber education. This is an area that has been worked on since my tenure, but it still needs a lot of work, as evidenced by my own family's prescriptions.

Second, we need to continue to keep track of the use of opioids and crack down on those who are using them inappropriately or prescribing inappropriately. We need to redouble our efforts to develop medications for pain and also behavioral therapies.

Here I would point to the PCORI Network and the NIH co-laboratory that just published a paper showing that cognitive behavioral therapy is effective for chronic pain. We still have a lot of work to do because we are not seeing a lot of these medications that are not addictive being developed at this point.

Then I would say, finally, we are all going to need to work together because the problems now with the explosion of this epidemic on the streets of America with these synthetic opioids is going to require that all of HHS work together. There is a concerted plan, and I would call your attention to it. I am all on board for the FDA to play its role in this plan.

The CHAIR. Okay, thank you. On another topic, right now we are seeing the Omicron variant of COVID–19 spread and quickly learning about its impact. As we have seen throughout this pandemic,

access to diagnostic testing is a critical component of our public health response, allowing the Government to understand new variants, respond quickly.

If confirmed, what would you do to make sure that the country is well equipped to handle future testing needs for COVID–19?

Dr. CALIFF. Well, I am a big data person and I think essential in the development of tests for a population as large as the United States, and as a matter of fact for the world, is that we understand the operating characteristics of the tests and the underlying technology.

I was just thinking about this yesterday because my son Sam was feeling kind of punky after his third—his booster dose of the vaccine yesterday and he stopped in at the local drugstore, got a rapid test. It was negative, and then we all felt Okay about Sam getting on the plane.

I think we have really got to redouble our efforts now with Omicron on the scene because we know it has a much higher rate of reinfection of people who have already been infected or in breakthrough infections and people that are vaccinated. So this—I am well aware of the issues with testing in general. It is complicated.

I can answer questions in more detail, but fundamentally we have got to work together to make the tests available so that they are not expensive. Every family should have a quantity of tests that they can use for purposes like Sam yesterday.

The CHAIR. Okay, thank you. I will reserve the balance of my time. We do have votes at 11 a.m.

Senator Burr.

Senator BURR. Thank you. Thank you, Madam Chair. Let me just note for Members that 55 percent of FDA's budget is approved through the appropriations process in Congress. 45 percent of the FDA budget comes from user fees. I would tell you this is an alarming trend that we have seen over two decades of the reliance on the industry to fund an agency that, quite frankly, Congress could fund.

Dr. Califf, you have been—you have had the benefit of a previous tour of the FDA. Should you get the opportunity to return, you will have more years of academic and industry experience under your belt and likely with more time to achieve your goals than the 10 months of your last term of service. What is going to be your biggest priority at the agency?

Dr. CALIFF. Well, Senator Burr, as we discussed in terms of priorities, obviously the pandemic is No. 1, and it is not just this pandemic. I was around for the wide guidance at the end of my tenure last time around, and I am fully aware of the need for the FDA to help develop platforms that will be essentially ready to go when emergencies come up.

We need also a workforce which is capable of working with those technologies. But in addition to that, as I said, we have got to find the right balance of protecting Americans in a safe way and being innovative in the development of products that can move along quickly. And essential in that priority is the development of a better evidence generation system. You yourself have advocated for more rapid approval.

If we do that, we have got to have a system that can keep track of the benefits and risk of the use of these treatments over time so that when we find something that is not so good, we stop using it. When we find it really is good, we got to use it much more often. And I can go into much more detail about how to go about that.

Senator BURR. I look forward to working with you on that. You have a history with the risk evaluation and mitigation strategy or REMS for the drug, Mifepristone. Many around the country have asked that you address this issue. Do you believe that the FDA needs to take any action to further weaken the REMS for this or similar drugs? Or can you reassure us that no changes are needed at this time?

Dr. CALIFF. Senator Burr, I appreciate the importance of this question. As you are well aware, a fundamental principle at FDA is that Americans should have access to drugs that are safe and effective for their FDA indicated use, and guiding those decisions is the best available evidence with core scientific principle, just like any other area regulated by the FDA.

I am aware, as are you, that FDA has filed a court document indicating that its review of the REMS stay on the Mifepristone is soon going to be available. As you know, in this position I am in now, I am not involved in those discussions and I can't predict the outcome, but I have great confidence in the FDA staff that they will use the latest available evidence and core scientific principles to make the best possible decision.

Senator BURR. More than 265 treatments and therapies have been approved under the accelerated approval pathway and have made a marked difference in cancer treatment. The accelerated approval pathway dates back to 1992, when patients diagnosed with HIV or AIDS had no effective treatment to help them. The accelerated approval pathway is a successful and important pathway at FDA. It brings us game changers faster.

It has recently been the subject of scrutiny, but I think it is one of the best ways to show that we are serious about breakthroughs and bringing new hope to Americans battling things like ALS, cancer, or Alzheimer's. Can you commit to me and to patients who may rely on cutting edge treatments that you will not support efforts to narrow this pathway or raise the bar for drugs to be approved under those pathways?

Dr. CALIFF. Senator Burr, first, let me just say that one great thing about the FDA is it is always under scrutiny from every angle. In fact, it is often said the best position for the FDA is when all sides are, I won't use the word, but are angry, I will just put it that way, about the decision. I think—I am a fan of accelerated approval for the right conditions. As you well know, I have spent countless hours with patient groups, people with rare genetic diseases, cancer, serious diseases for which there is no treatment.

American people prefer to get earlier access. But I would also stress, as we discussed in your office, it doesn't stop there. The very fact of accelerated pathway means that we are accepting that there is more uncertainty, and the FDA has tremendous latitude about the decision it makes with those pathways. And that means we have got to have a better system to evaluate these products as they

are used on the market. And I think there are ways that we can do that.

Now, technology is making this possible in a way that just wasn't possible before, so I would really look forward to working with you on that part of it also.

Senator BURR. I look forward to working with you on those post approval reviews as well. Thank you, Madam Chair.

The CHAIR. Thank you.

Senator Sanders.

Senator SANDERS. Thank you, Madam Chair. And Dr. Califf, thanks so much for being with us and thank you for your years of work as a physician. Dr. Califf, I am sure you were aware, the pharmaceutical industry is probably the most powerful special interest here in Washington, DC. It has spent over $4.5 billion on lobbying and hundreds of millions of dollars in campaign contributions over the past 20 years, not to mention the huge amount of money it spends on advertising.

As Senator Burr mentioned, on top of all of that, 45 percent of its budget comes from user fees. And one of the major reasons why the pharmaceutical industry, among many others, is so powerful is its close relationship with the FDA and other regulators in Washington. As you may know, over the past 40 years, 9 out of the last 10 FDA Commissioners went on to work for the pharmaceutical industry or to serve on a prescription drug company's Board of Directors.

A gentleman named Curtis Wright, who was not a Commissioner but a high ranking official, in 1996, left the FDA to receive a $400,000 compensation package at Purdue Pharma, less than a year after he approved OxyContin with a label that said it was "very rare" for patients to become addicted to that opioid. Tragically, obviously, that was not the case. Unfortunately. Dr. Califf, you are not the exception to that rule.

Since you left the FDA in 2017, you have made several hundred thousand dollars from pharmaceutical companies and have received consulting fees for Merck, Biogen and Eli Lilly. According to your financial disclosure form, you own up to—you currently own up to $8 million in stock of major pharmaceutical companies.

At a time when the American people are outraged by the high cost of prescription drugs, deeply disturbed about what happened with Purdue and OxyContin, what kind of comfort can you give to the American people when you have been so closely tied to the pharmaceutical industry yourself? How are they going to believe that you are going to be an independent and strong voice against these enormously powerful special interests?

Dr. CALIFF. Senator Sanders, I do appreciate your concerns and I am totally with you on the concept that the price of pharmaceuticals is way too high in this country. I have a public record on this. It is in print in a number of articles that have been written. With regard to my own status, I am a physician first and foremost. In the early part of my career, I spent working in intensive care units taking care of——

Senator SANDERS. I don't have a lot of time. I apologize. Could you answer the question? You own millions of dollars in stock. You are going to consultant to the industry. How can the American peo-

ple feel comfortable you are going to stand up to this powerful special interest?

Dr. CALIFF. Senator Sanders, I have a history of doing that. But I would also point out this Administration has the most stringent ethics pledge in the history of administrations. They have reviewed my status. I have agreed to the ethics pledge, and FDA and HHS have excellent staff whose job it is to make sure that those ethics pledge——

Senator SANDERS. Thank you. Let me ask you another—I apologize. There is not a lot of time. According to the FDA's website, its mission is to "make medical products more effective, safer, and more affordable, more affordable." If confirmed, what would you do to make the outrageously high cost of prescription drugs in this country more affordable?

Do you believe, for example, that when the Federal Government pours millions and millions of dollars into the development of a drug, we should have a reasonable pricing clause which prevents the drug companies for charging, for charging consumers what they have already paid to develop? Do you believe in reasonable pricing?

Dr. CALIFF. I certainly believe in reasonable pricing. And four specific things, I will just quickly mention, just rail them off. No. 1, we need to develop even more robust generics. 90 percent of prescriptions are generic. The biosimilars program needs to continue to develop that scenario where——

Senator SANDERS. But do you believe—again, I apologize, just not a lot of time. When the Federal Government puts money into the development of a drug, should consumers be protected from high prices, yes or no?

Dr. CALIFF. In any situation, consumers should be protected from high prices.

Senator SANDERS. Should Medicare be able to negotiate prescription drug prices?

Dr. CALIFF. Yes, and I am on record. There was a policy of the previous Administration——

Senator SANDERS. You think Medicare should do what the Veterans Administration does?

Dr. CALIFF. Well, I can't say exactly what the Veterans Administration——

Senator SANDERS. VA pays half the price that Medicare pays for its drugs. Should Medicare do what the VA——

Dr. CALIFF. I am on record of being in favor of Medicare negotiating with the industry on prices.

Senator SANDERS. Thank you very much.

The CHAIR. Thank you.

Senator Romney.

Senator ROMNEY. Thank you, Madam Chair. Appreciate the chance to hear from you, Dr Califf. And we had the chance to discuss some of these things when we were together in my office and I would like to raise them again, in part so they are on the record, but in part also to elaborate on them. One is with regards to two clinical trials.

There is a perspective that drugs that are approved are, the clinical trials are paid for by the industry, by the drug companies themselves, and that the Government itself doesn't have the occa-

sion to develop its own clinical trials and to promote the evaluation of a product which the Government may think is of interest, but there is no company that is interested in pursuing it.

Does the Federal Government fund clinical trials at all? And No. 2, should we do more of that? And if so, how?

Dr. CALIFF. Well, first of all, thank you and I enjoyed our discussion. I hope the Government will continue to do what it has done, is to fund clinical trials. I, over time have been one of the highest funded NIH investigators doing independent clinical trials when I was in academia.

As we discussed, the industry does fund its own clinical trials for its own purposes. But there are many issues of public health, essential public health importance where only the Government can fairly ask the question. And your institutions on Utah have been key contributors to those clinical trials that have been done. I would like to see more Government funded trials so that we ask the unbiased questions about which therapies are the best for which people.

Last, I will mentioned PCORI, the Patient-Centered Outcomes Research Institute, which Congress graciously just refunded for 10 years, is created just to do that particular part on behalf of patients. As a doctor, the most common question I got is which treatment is best for me, and that takes comparative clinical trials that the Government is very well suited to do.

Senator ROMNEY. Thank you. I don't happen to be a believer in this horse deworming product known as ivermectin. But it is my recollection that is something which is actually going through clinical trials funded by the Government, not by the industry. Is that correct?

Dr. CALIFF. That is correct. The NIH is funding two large trials right now, one of which using a network which I helped create with the NIH and this Patient-Centered Outcomes Research Institute. So I think we also see treatments, and I made the point in my opening statement. Most of what we develop, no matter how good the science looks, turns out to have risks that supersede the benefit.

Only 10 percent of drugs that make it into human clinical trials actually make it to market because of this problem. So we have got to have an open mind. We have got to do the trials and then we have to follow the science, follow the data.

Senator ROMNEY. Thank you. I was made aware of a practice that perhaps you could elaborate on, which is that a product may be approved for usage by a physician but limited in when it can be used or how it can be used.

I am thinking with regards to monoclonal antibodies, it was related that individuals in a hospital with advanced COVID had been in the hospital for several days, wanted to get a monoclonal antibody treatment, but was told you can't get that, we won't allow you to have that in the hospital, the FDA doesn't allow us to treat you with monoclonal antibodies, even though at the beginning of the disease they would have been potentially effective. Later on, we don't think they are, so we won't treat you.

That seems to be an awfully unfair way to deal with someone who is in a life threatening circumstance. Is that the correct prac-

tice? Is that a correct understanding rather of that practice? And does it make sense? And if so, why?

Dr. CALIFF. Well, I will try to be brief and the answer here. First of all, let me just say I followed this closely because we knew monoclonal antibodies were highly likely to be effective against SARS-CoV–2 because they worked for the first SARS epidemic, which fortunately was stopped early and never became a global pandemic.

As these drugs were developed, it is an amazing effect of 90 percent reduction in death and hospitalization, but most effective if used early. And that really should be the focus. And I think that is the basis for which the practice that you described may have evolved. Very effective, if at all, in people who go—as you know, you get sick with the virus and then a week or 10 days later, you may get sick enough to enter the hospital. By that point, there is much less effect.

Now, the specific practice of preventing prescription of antibodies, I am not aware that is happening, but it may be, and I think that would need to be looked at in context. There are some people who don't develop an antibody response where the treatment may be effective.

Senator ROMNEY. Thank you. I have got more questions, but my time is up. Madam Chair, thank you.

The CHAIR. Thank you.

Senator Casey.

Senator CASEY. Thank you, Chair Murray. Doctor, thanks for your willingness to commit more time to public service at the FDA. We are grateful for your willingness to do that. I wanted to raise at least two subjects with you. One is over the counter monograph reform and then also antimicrobial resistance.

But first, on the over-the-counter monograph reform, I appreciate the commitment you expressed during our meeting with regard to implementation of the reform law that was passed last year as part of the CARES Act, and I also appreciate the work and the challenges that FDA confronts with implementation.

We are grateful for the steps that have been taken so far to implement the law. This—the law, as you know, included new tools for both the FDA and the over-the-counter industry to facilitate innovation accompanied by appropriate regulatory oversight. This includes the user fees that accompany the regulatory authority to enable FDA to build out a modern over-the-counter regulatory system with the necessary human resources.

I appreciate the early implementation milestones, such as the deemed administrative orders being issued. So here is my question, as this implementation continues, will you commit to the following, No. 1, ongoing communication and transparency with Congress? No. 2, transparency with regard to—with the public health and industry stakeholders?

Dr. CALIFF. Yes. Thank you, Senator, and thank you for getting this through. It is—in the world of regulation, this is pretty exciting. And I personally visited the drug store early this morning to get an over-the-counter medicine, and it was noticeable to me as Commissioner last time around that we needed to do something so that these monographs could be updated as innovation is made, but

we also were empowered to look at the safety of these over-the-counter products. So it is really appreciated, and I do commit to transparency and discussion with you and others in Congress.

Senator CASEY. Thanks, doctor. Next on antimicrobial resistance, this is an issue that presents right now urgent public health challenges. According to the Centers for Disease Control and Prevention, there are more than 2.8 million antimicrobial—antibiotic resistant, I should say, antibiotic resistant infections in this country every year, causing more than 35,000 deaths.

This Committee has tackled this issue in a number of ways over the years, including the passage of the so-called GAIN Act, the Generating Antibiotic Incentives Now Act, and that was back in 2012. The GAIN Act gave FDA new tools and provided new incentives to drug developers to encourage them to meet this urgent public health threat. Yet since that time, we have made very little progress in getting new antibiotics approved to combat these drug resistant infections.

Numerous experts have expressed concerns that the COVID–19 pandemic could exacerbate the spread of antimicrobial resistant infections. And I want to note the work with Senator Cassidy on this. We have been able to work with him on this and other Members of the Committee. What do you see as the barriers to more antimicrobial drug development? And how would you work to support that drug development within the FDA, if confirmed?

Dr. CALIFF. Thank you for raising this issue. And while we are so consumed with the pandemic right now, we cannot lose sight of this other threat. In my lecture after leaving the FDA, I gave, safety and effectiveness of medical products, food, tobacco and always put in preparation for emergencies.

At the time, 5 years ago, people sort of scratch their heads like, what is that? I think we all know what that means now. But we can't lose sight of the fact that we could get a super resistant bug, and if we don't have antibiotics on the shelf that are ready to go, we are going to have a big problem.

It will be difficult, if not impossible, to treat. This involves a whole variety of things, one of the most important of which is one health, the combination of animals and human evaluation, because many of these resistant bacteria are developed in animals that are treated with antibiotics.

But in addition, there is what you mentioned. We have to have a system of developing antibiotics, essentially not intending to use them because you want to hold them in reserve. And there are several mechanisms to do that I would look forward to working with you on.

One pathway you have already passed in Congress and that is in motion now, but we are going to have to do a lot better or we may be taken by another surprise, and we don't want another one like the current pandemic.

Senator CASEY. Thanks, doctor.

The CHAIR. Thank you.

Senator Braun.

Senator BRAUN. Thank you, Madam Chair. Dr. Califf, enjoyed our conversation in my office not too long ago, and we covered a broad array of topics. I have been one interested in reforming

health care in general to add transparency, competition to it, FDA specifically, and I think we did cover some discussion on making it more agile, especially on maladies that don't have really good treatments out there.

You said you would be amenable to that. I like to hear that. This is a question I have asked since the origin of the COVID kind of navigation, and now we got a lot of data. We are lucky that we did have Warp Speed. We got the vaccine done. Looks like with variants, they are going to be renditions of it that we still need to tackle.

Whether vaccines will be the only leg that we use—I have been a believer that it needs to be broader. In the subject of therapeutics, are you willing to put the same interest in developing therapeutics, especially in light of the fact that some either choose not to get it for the wrong or right reason?

Where does that fit in your opinion in terms of the relative importance, especially given the fact that it looks very difficult logistically, we will get the world vaccinated in a way to suppress variants? How important are therapeutics, and where will you be, your posture in terms of promoting that second leg, if not a third one down the road in terms of protecting against it in the first place? Focus on the therapeutics.

Dr. CALIFF. I am a cardiologist, so we are fairly well known in the medical community as being aggressive people over the garden therapeutics, and I think it has made a huge difference in heart disease. We have drugs and devices, many of which I have worked on in my career, and I think the same holds here. Vaccines are far and away the first line of defense, in addition to the behavioral measures that we all know about. But for people who were unlucky enough to get infected, particularly those that are high risk, the therapeutics are absolutely essential.

Already made the point with Senator Romney, the therapeutic, antibiotics have a 90 percent effect, and now it looks like we have oral antivirals that may also be in that category.

We have got to stay on top of this because the virus doesn't really care about us, it is mutating constantly, and we have got to have platforms that will produce therapeutics just in time for the variants as they come up. But so, therapeutics is a big part of the FDA. It is a big part of my history, and I will definitely work hard on this.

Senator Casey. I think from what you said there that you are willing to acknowledge that it is going to have to be a significant part of how we tamp this down over time and I am glad to hear that. Another question I have. Under your leadership, in 2016, the FDA weakened the risk evaluation and mitigation strategy on protocols on Mifepristone—hard to pronounce, but a drug that is used, early in the stages of when you are entertaining an abortion.

A recent study analyzed 423,000 taxpayer funded abortions between 2002 and 2015, and I have got a question. Do you think that we need to be in that relaxed kind of interpretation of that particular approach? Or is this something you are going to listen to current information and technology on so that you give a full kind of consideration of that particular methodology on abortions?

Dr. CALIFF. Well, as I have already discussed with Senator Burr, I do appreciate the question. There is a document filed by FDA in court about the evaluation of the data on Mifepristone. And, the re-evaluation is imminent. I am not involved in that particular re-evaluation, but I can assure you the staff will be looking at the latest data and applying the best science and make the best possible decision. I have confidence in that staff, and I know them well.

Senator BRAUN. I think that is in the context of what we are seeing, even with what the courts are taking up in terms of trying to get the proper balance on Roe v. Wade and that issue is going to be out there. And I think to many Americans, it is an important, including the question I just asked.

Madam Chair, I ask unanimous consent to submit for the record the testimony of an individual that experienced complications resulting from a chemical abortion drug.

The CHAIR. Without objection.

[The following information can be found on page 93 in Additional Material:]

Senator BRAUN. Thank you.

The CHAIR. Senator Murphy.

Senator MURPHY. Thank you very much, Madam Chair. Dr. Califf, thank you for your continued willingness to serve the country. I am going to submit two questions for the record that I hope you will take a hard look at. One, on the continued delay in regulating medical gases. This is something that there is bipartisan interest in. The current regulatory system just doesn't work for medical gases, and we would love for you to take a look at how we can expedite that process. And second, a question for the record on the issue of counterfeit medical products.

We are thinking about bipartisan legislation here that would provide some new authorities to crack down on counterfeit products. We have obviously seen a disturbing growth in the distribution of counterfeit devices during the pandemic, PPE and testing kits at the top of the list.

But the two questions I would love to have you answer in person are on mental health drug development and drug shortages. On this question of mental health drug development, it is pretty stunning the slow pace that we have seen of new and transformative drugs in the mental health space.

Right now, there are some products in the pipeline like for schizophrenia. But overall, relative to the need, we aren't seeing enough new innovative products come forward. And that has to do in part because of the complex patient populations that we are talking about here that can make research and clinical trials and data collection more complicated.

You have written about the need to streamline the clinical trial process and the opportunity for digital technology to expand people that can participate in trials. Do you think that reform can help unlock more research and more clinical trials for individuals with behavioral health needs?

Dr. CALIFF. I mean, the short answer would be yes, but I would like to give a slightly longer answer. I won't take too much time because this is an area of great passion for me and experience. I don't think people in America realize enough that before the pan-

demic, we were experiencing an unprecedented reduction in our life expectancy in the U.S., largely driven by the opioid crisis, that is addiction, and also by suicide.

In addition to common chronic diseases, it is often driven by people who are in despair and not taking the best care of themselves. And we also haven't talked enough about the fact that in addition to the disparities that we all know of, with up to 10 year difference in life expectancy according to race and ethnicity, we have an enormous urban, rural issue in this country where the rapid decline in life expectancy are people in rural America.

I don't see any way to connect to everybody in America except through digital technology, but it should be supplemented by people on the ground who help people deal with digital technology in the local community.

I see this as the way forward. We started a drug addiction program in Dayton, Ohio, where the highest mortality rate per population was occurring. And in that take all comers program, the ability to use telehealth to reach people in rural Ohio has made an enormous difference. So that is a longer answer to say, yes, let's get on it. We need to do something about this.

Senator MURPHY. Well, and I appreciate that answer. I want to make sure that we are, focusing on more widespread and traditional behavioral health disorders, not simply on addiction, where we need—drug development is covering both. But it is still pretty stunning that in the area of treating depression today, we are living in a trial and error world.

We still lack the data necessary to be able to know with the kind of certainty with like what drugs are going to work right off the bat. And a lot of patients have to try and fail on multiple therapies before they find the one that works. And so I look forward——

Dr. CALIFF. I have led my own number of failed clinical trials trying to develop new treatments for depression specifically and also for anxiety. So we have got—I completely agree, we have got to address these very prevalent mental health conditions directly.

Senator MURPHY. Quickly on the issue of drug shortages. In 2012, the FDA Safety and Innovation Act gave FDA new tools to address drug shortages. And I just want to make sure that we are looking into the future where we might have increased tensions with countries that are critical to our drug supply chain. Do you think that FDA has the authority it needs to really think 5, 10, 15 years down the line to look at shortages that may result based on changes in our relationships with economic allies?

Dr. CALIFF. Senator Murphy, I really appreciate that question. And let me just say I was serving on the National Academy of Medicine Supply Chain Committee, which is due to produce a report any minute now. I can't reveal what is in the report but let me just say I don't think people are aware of the tenuousness of our current supply chain.

We have to have transparency and build in resilience, or we are going to be at risk. And in fact, if you talk to hospitals and medical practices, it has already happened that we have fallen short of critical supplies periodically. So we really need to work on this.

The CHAIR. Senator Cassidy.

Senator CASSIDY. Hey, Mr. Califf, nice to see you.

Dr. CALIFF. Great to see you.

Senator CASSIDY [continuing]. From afar. I am told that—I was out at another Committee hearing, but I am told that Senator Sanders asked if you support negotiation and you agreed. Now, do you think that the FDA has a role in this negotiation? Let me first ask you this.

Dr. CALIFF. No, and we were a bit short on time, so I was trying to compress my answers. I mean, I have a published record saying, I think negotiation is a good idea, but that is not the role of the FDA. So that is the answer.

Senator CASSIDY. That is fine. I also want to associate myself with Senator Casey's remarks about the work we are doing on antimicrobial resistance. And I think you—I know you will be very aware of that, and how do we come up with ways for these necessary antibiotics to somehow have a business plan which works, so just to mention that as well.

Dr. CALIFF. I really appreciate your help with that. And I remember in 2016 sitting there with all of the relevant agencies and you are trying to keep track of the microbial underpinnings on a global basis because we are all connected, and we, it is a great place for big data if you love the science, but we have got to figure out how to get a handle on this.

Senator CASSIDY. You had mentioned in a conversation we had prior to this that I had raised the issue, and I want to follow-up on it just to set the stage, we know that complex generics, if I remember my term are correct, that for example the EpiPen, that you could change whether or not you turn the device to the left or to the right, and that would give a lease of life of exclusivity upon the product.

Dr. Gottlieb suggested, your predecessor, to allow equivalency between, Okay, you can—you don't have to turn left or right, it can still be considered the same product, but with alternative instructions. You had mentioned great idea, but that FDA needed tools to allow that to be implemented. We didn't follow-up in the conversation. Is there more you want to say to that?

Dr. CALIFF. I would just say, it is going to take a lot of work for me to get completely up to date on all the current tools that are at our disposal. But your point is so well taken. I think you and I agree that what we want to reward is innovation and creating new things that make a difference in people's health. People should do well if they do that. But having legal tricks that extend patents and reduce competitiveness, I just don't think that's a good idea under any circumstances.

Senator CASSIDY. Let me ask, how long would it be until you think you could come back to this Committee with recommendations as to how we can address those legal tricks to give FDA the ability to offset them, if you will?

Dr. CALIFF. Well, I would say to give a specific time, but it should be short. I mean, I am not ignorant on the issue, and we had a good list in 2016, but I think a number of those things on the list have already been taken care of, like the buying a generic company to prevent the competition from occurring. I think these things you all have already helped with, so I want to make sure

I have got the updated list. It should be fairly, very quick, I would think.

Senator CASSIDY. Next—thank you, I look forward to that. Next, we had spoken again offline about the accelerated pathway, and how the Biogen drug for Alzheimer's obviously addressing the need, which is devastating, but there is a lot of concerns about efficacy, safety, and cost. And you had mentioned using big data in order to have a quicker answer on drugs such as this. I would like you to elaborate on that, please.

Dr. CALIFF. Sure. Well, we have essentially 300 million plus Americans with electronic health records, and our health data is being used all the time in clinical practice. A lot of my career has been on the issue of how do we use that data, organize, curate it, make it useful for research.

It sometimes startles people when I say the data is good enough to use in clinical practice, as you well know, but not good enough for research, and people say, wait a minute, how can that be, that it is good enough for me, but not good enough to draw a conclusion. I think we are well down the road now and having a functional system, but also want to assure people I am not talking about willy nilly analysis of data.

I am talking about, well, planned studies, frequently the use of randomization. And if we look at the UK during the pandemic, that is what they did. They organized as a country, they took on the big questions, and they have answered a lot of questions very succinctly, with the advantage they don't have to spend a ton of money collecting what is already in the electronic health record.

Senator CASSIDY. Let me ask you, do you need more—do you need different rules that we have to give you? Or can you do that with existing authority?

Dr. CALIFF. I think the FDA has adequate authority, but I think the system, because this takes many players. CMS has to be involved. The private health sector has to be involved. And I think the most important thing is to develop a system that gives Americans trust that their data can be used not for someone else necessarily, but for their own benefit.

I mean, if I had a heart attack today, I would feel a lot better if I knew how all the other people like me had faired with the different treatments. And so it is in my interest to share data, but we got to develop—I think we do have work to do to develop a system that Americans will trust to allow this to happen.

Senator CASSIDY. I look forward to your further thoughts on how to develop that system, and I thank you for your vision. I yield.

The CHAIR. Thank you.

Senator Hassan.

Senator HASSAN. Well, thank you, Madam Chair and Ranking Member Burr. And I want to thank our witness and your family for your willingness to serve. Dr. Califf, I want to return to the topic of opioids. In 1995, the FDA first approved OxyContin, as you have acknowledged, a very powerful opioid drug. Since then, more than 500,000 people have died from opioid related overdoses.

In 2020 alone, over 357 granite staters in my home state lost their lives due to opioid overdoses, and tragically, many people first became addicted to opioids through a legal prescription for

OxyContin or other FDA approved drugs. First question, did the FDA make a mistake when it approved OxyContin in 1995?

Dr. CALIFF. I think if we look back, approving OxyContin with no long term studies and no assessment of the addictive capabilities is something that could have been done differently.

Senator HASSAN. In 2001, the FDA revised the OxyContin label to indicate that the drug should be used not just for short term pain, but when a "continuous around the clock opioid analgesic is needed for an extended period of time."

In other words, the FDA specifically indicated OxyContin for long term use to treat chronic pain. Former FDA Commissioner David Kessler, who led the agency in 2001, has since said that there are no studies on the safety or efficacy of opioids for long term use, and has called the FDA's 2001 decision a mistake and a, "blank check" for the industry. Do you agree with that assessment?

Dr. CALIFF. Well, the only little part of I disagree with is there are now long term studies underway, but at the time, he said, I think that it was accurate, and it could have been done differently. I mean, I am an evidence based person, and if we are going to instruct people to take drugs for long periods of time, we need long term studies.

Senator HASSAN. Well, look, it is an old adage, but it is worth repeating, the first step toward fixing a problem is admitting that you have one. Repeatedly, I have asked FDA officials about this, and I get this kind of vague answer about whether the 2001 relabeling was a mistake. And its failure to admit to having created problems for more than 20 years is part of why we have an opioid crisis in the first place.

It is still troubling to me that we don't have direct acknowledgment by FDA and FDA officials that they made mistakes and that in 2001 the decision to re-label created an even worse problem. Let me just move forward to one other thing, you became FDA Commissioner in 2016.

By that time, we did know an awful lot about the addictive nature of OxyContin and the problems with the label from 2001. Why didn't you take action to change the OxyContin label when you led the FDA in 2016?

Dr. CALIFF. Well, what I did was to, several things, one is to take—support these long term studies that needed to be done to get the evidence and also contract with the National Academy of Medicine to reset the format for the evaluation of opioids. The tradition of FDA is to evaluate risk and benefit for the person for whom the drug is prescribed. This affects many other people in society and that was successfully done, so I do believe it has set the framework for that.

Senator HASSAN. But doctor, when you listed in response to Senator Murray's question, when you listed what we need to do going forward on opioids, you said we need to reassess some things, we need more prescriber education. You cited your own family's experience with getting a 30 day prescription for opioids for minor surgery. If the label were different, the doctor wouldn't have prescribed that family member the 30 day prescription. So explain to me why we shouldn't aggressively be pursuing relabeling.

Dr. CALIFF. I think as the evidence comes in, we are going to need to aggressively look at relabeling. And that was the purpose of setting a different framework so that we would have a legal framework for doing that.

Senator HASSAN. The evidence has been here for a long time. It is the evidence of thousands of people, hundreds of thousands of people dying in this country. It is the evidence that I see when I go to the funeral of a constituent who has been in recovery multiple times and has relapsed.

It is the evidence that I see when I go to the funeral for that constituent's sister and listen to a mother who has lost two adult daughters to this illness despite their repeated attempts to enter recovery. There is plenty of evidence about what we need to do about this epidemic and the FDA needs to take the lead. Thank you, Madam Chair.

The CHAIR. Thank you. I am—we have three votes, and I am going to go vote, and turn the gavel over to Senator Burr. The next two Senators will be Senator Tuberville and Senator Smith.

Senator TUBERVILLE. Thank you, Madam Chair. Thank you, Dr. Califf, for being here today and bringing your family, and being part of this and continue to want to service such a tough time in our Country. Very quickly, the State of Alabama. We have lost people in our state because of testing. We don't get to them quick enough in the rural areas. What is your suggestion on that?

Dr. CALIFF. Well, I mean, we have got to make tests available and either free or low cost, and they need to be readily available in the person's home. There is also just a tremendous amount of education that we need to do to make sure that people are aware that when they have symptoms or when they think they have been exposed, they should get tested because of the extreme risk, particularly if their high risk.

In the rural population, as I have already stated, there is a huge amount of common chronic disease that really means that we have a lot of high risk people in the rural areas. And I wouldn't understate the critical importance of education programs for the primary care practices in rural areas. These folks are overwhelmed and incredibly busy, and we got to catch people early on because these treatments that we talked about are highly effective if used early.

Senator TUBERVILLE. Yes. While we are on this subject, what is your thought about this new pill that they have come out with, I forget which company, this new therapeutic that they are saying is very effective?

Dr. CALIFF. Well, there is the saying in God we trust, all others must bring data when it comes to the FDA. So the press releases out, I think, this morning on something that looks really exciting. And there is every reason to believe that a direct antiviral should work because it works in other viral diseases.

I really look forward to the FDA's evaluation of the actual data, which I think is going to be done very quickly, just like the other therapeutics. And the idea that if you are unlucky enough to get infected, let's say even if you are vaccinated, the idea that there is a 90 percent effective treatment is truly exciting.

Senator TUBERVILLE. In my former job, the last 10 years of my 40 years of coaching, I would bring players in, and more and more

each year, a higher percentage of kids would come in taking drugs. You would bring 25 in, 20 years ago, there might be one, maybe two that take an insulin or something like that.

Now you bring 25 and half of them are taken attention deficit drugs like Ritalin. I think we are overprescribing these drugs. I think we get them involved in drugs at too early of an age. What are your thoughts about these mental health drugs that Senator Murphy was talking about?

Dr. CALIFF. Well I think there is sort of a Goldilocks thing here, not too big, not too small. And we have got to find the right place for each treatment, for each type of problem that people have. And the only way we really know that is to do the clinical studies, get the evidence, and then we know what the risks and benefits are. Too often with children, we have not had the right evidence early on and the docs are guessing, the prescribers, maybe a nurse practitioner are guessing about what the best treatment is.

I mean, my answer this week is, got to double down on getting the evidence. We have talked about some of the ways of doing it already this morning using electronic health records and such. Once we have the evidence, if someone is prescribing—I think in the example, the Senator Hassan said of the opioids, if someone's prescribing a bunch of unnecessary stuff, we need to have a system that deals with that effectively.

I think almost all the drugs on the market, they—the drugs have been shown to be effective for an FDA approved indication, but when they get out beyond those indications, we have got a lot of work to do to get the right evidence.

Senator TUBERVILLE. Thank you, Dr. Califf.

Senator BURR. Senator Smith.

Senator SMITH. Thank you very much. Dr. Califf, welcome to the Committee, and welcome to your family, and thank you for your willingness to serve again as FDA Commissioner. And I appreciated our conversation of a couple of weeks ago, I think it was now, and I just want to say I particularly appreciated your commitment to advancing equity. I think that is a matter of such great importance. I want to follow-up first, though—I am going to try to touch on two or three things.

I want to follow-up first on a question that Senator Murray brought up, touching on how we can get more rapid COVID–19 testing to the market. As COVID–19 becomes more endemic, affordable, available, and in-home rapid testing is going to be so much—so essential. And the FDA has taken steps to streamline the review process for authorizing COVID–19 tests, including rapid tests.

Some policy folks are arguing that we should be reclassifying rapid COVID–19 tests as a public health tool rather than as a medical device, and that this would help to increase supply and reduce prices. So I am wondering if you could, Dr. Califf, could you based on your experience, what do you think about this idea? What do you see as the downsides? And what more do you think that we could do to speed up the supply and lower the price of rapid tests at home?

Dr. CALIFF. Well, that exact solution—well, first of all, thanks for the question. I think you may not have been here when I men-

tioned my son, Sam, back here, got two rapid test yesterday because he wasn't feeling too good after his booster shot and it was negative. So I fully personally appreciate the impact of having readily available rapid tests. But that specific solution, I don't think it solves a problem. It may be one pathway, I would have to study it. What I do know, I mean, I started my career evaluating cardiovascular tests. This was in 1978. It was a long time ago.

But the principles are the same, and the purpose of the test is really important. A test to screen for a disease, a test to diagnose the disease, a test to determine the prognosis, what is the likely outcome, the operating characteristics that you measure are different. And we do need to have a system, and I know Senator Burr and others are working on this, now we need to have a system that takes these different purposes into account.

Just like with a drug, a drug may have a use and several different indications, and the dose may even be different in different indications. So we got to have a flexible system that takes these things into account and an evidence generation system that makes sure that when we are using it for one purpose or another, we actually understand what the test result means.

Senator SMITH. If you are confirmed as FDA Commissioner, will you commit to reviewing the current process for authorizing tests and take steps to streamline this process, and make sure you let us know if there are things that we need to be doing here at the Committee to support that effort?

Dr. CALIFF. Yes. Yes, I would very much look forward to working with you on that, and I would actually get back to where I started my career, so I would find it in an already sort of way pretty, pretty exciting.

Senator SMITH. Thank you. That is good. Dr. Califf, while the FDA doesn't set the price of prescription drugs, the FDA has significant power to bring more low cost generics and biosimilars to market. This has been a big priority of mine. In fact, the first bill that I introduced when I came to the Senate is a bill to prevent parking of—the parking situation that we have.

In fact, this is a bipartisan bill that I have with Senator Braun, and it would prevent generic manufacturers from getting, and name brand manufacturers, from gaming the system and help to streamline getting those generic drug approvals done. Could you talk a little bit about how you would use the tools at your disposal at the FDA to prevent anti-competitive behavior like parking in the prescription drug market?

Dr. CALIFF. I think I have already mentioned, in 2016 we had a long list of ways pharmaceutical companies could extend the patents or otherwise get around the intended move to generic status after an appropriate period of patent exclusivity. And I think there is no other way than making a list, and it is a little bit like Whack-A-Mole. You have to—there are really smart people on the other side looking for ways to circumvent the rules.

You got to be on your toes, and then in some cases, FDA has the same power to make a difference. And in other cases, it would involve something that we would need from Congress to help take care of it, as in the case that you mentioned.

I would also mention, I am very aware in the supply chain issues that we have got to shore up the generic supply chain while we are also reducing the costs. And that is a big issue we need to pay attention to.

Senator SMITH. I absolutely agree with that. In the interest of time, I am going to submit for the record my final question, which is around how to address the need to include more pregnant women in clinical trials. And I will submit that question to you. Thank you.

Dr. CALIFF. Thank you. I want to take a quick second and say that, as you know, I work very hard on including children and clinical trials, and that work is getting better and better. Pregnant women is a big frontier. It is a very high risk situation.

Everybody is concerned. But if we don't do the studies, we end up with, like my daughter, who I mentioned had congenital heart disease. I have a granddaughter sitting back here, too. But when you have a chronic disease, you need to take medicine for it, even if you are pregnant. We have almost no studies that addresses those issues. So, I would really look forward to working with you on that issue.

Senator SMITH. Thank you very much. Thank you, Mr. Chairman.

Senator BURR. Senator Collins.

Senator COLLINS. Doctor, I was very pleased to hear you say twice this morning that your first priority is improving emergency preparedness so that we are better able to counter the inevitable next pandemic that comes our way. As you know, from our discussion, for a number of years, I have been very concerned that the United States drug market is increasingly reliant on the manufacture of active pharmaceutical ingredients at facilities overseas.

In fact, the FDA in 2019 testified that 72 percent of the facilities that manufacture APIs are located overseas, a lot of them in China and in India. In addition, we know that China has virtually cornered the market on manufacture of the antibiotics. I am very concerned that we see, as we saw with India, when there is a pandemic like COVID that countries began to hoard medicines that were destined for our markets.

I strongly believe that part of reforming the medical supply chain has to include incentivizing manufacturers using both carrots and sticks to locate their facilities in the United States, starting with the 100 essential medicines list. And perhaps we could link it to participation in the VA health program, for example. Perhaps tax incentives are needed. What are your thoughts on our vulnerabilities in the supply chain?

Dr. CALIFF. Thank you, Senator Collins, for the question. And as I have mentioned already, I served on the National Academy of Medicine Supply Chain Committee, which is about to come out with its report, so I don't want to say too much about the specific recommendations there.

But your facts are correct, and in the discussion I just had with Senator Smith, the active pharmaceutical ingredients are not just for innovator drugs that we think about, but also for generics, where often we don't have enough competitive entities in what has become sort of a commodity business.

We need a number of steps to make the system more resilient. Purely on-shoring is probably not the complete solution, but it is a part of it that is significant. But we need the supply chain to be secure and resilient in multiple directions, and a transparent system for knowing where things are in the supply chain, which we currently don't have.

I would mention one other thing, manufacturing in places and exciting technology that people have been working on and the idea that you can make a pill now with a small machine in a local area is something that I believe is coming, and we need to accelerate that as quickly as we can.

Senator COLLINS. In 1997, as a new Senator, I founded the Senate Diabetes Caucus, which my colleague Jeanne Shaheen co-chairs with me now. And it was after meeting with children with Type I Diabetes and their parents. And in the years subsequent to that meeting, there have been many advances in technologies such as continuous glucose monitors and far better pumps and a closed system. But there is still not a cure or disease modifying therapy yet approved for Type I Diabetes.

This year, the FDA has reviewed and held two advisory committee meetings for therapies for Type I Diabetes. One is a biologic that may delay the clinical onset of Type I by as long as 3 years in those at high risk. The other is cellular therapy made from donor pancreas for those who suffer from severe hypoglycemia.

In addition, there have been press reports that claim an individual has been cured from Type I Diabetes as result of new therapy. How would be FDA under your leadership continue to foster cutting edge science at the various centers we have created for Type I Diabetes therapies and devices?

Dr. CALIFF. Well, thank you for that, and let me just say that it is exciting. These two types of diabetes, which are different in terms of their origins and the idea that you could cure a person with Type I Diabetes, which has been a lifetime consignment to insulin therapy up until now, is very exciting.

I think we would like to continue this very healthy relationship between the patient community, the industry that makes products, and the regulators who have to determine if the products are safe and effective. And let me just point out, I think this is actually a paradigm. Multiple myeloma, which my mom had, or cystic fibrosis would be other examples where when you have an activated patient community with a group of families that are dedicated, it creates a very different situation where investment comes into the area.

People think of new therapies because they know that people are going to participate in the clinical trials and the turnaround and getting the evidence is quick. And then when practitioners go to treat the disease, they can have confidence they are doing the right thing because they have strong evidence.

I would frankly love it if more people copied that model, and it bothered me a lot at FDA when I would work with diseases that had no effective advocacy because they couldn't benefit from the kind of things that you created.

Senator COLLINS. Thank you.

The CHAIR. Senator Rosen.

Senator ROSEN. Thank you, Madam Chair. And thank you, Dr. Califf, for being here and for your willingness to serve. We really appreciate that. I want to go over telehealth and remote monitoring for a minute, because of course, as we have seen throughout the pandemic, telehealth has become more important than ever for improving access to care, especially among our rural and our underserved areas. It is critical that agencies work together, like you said, to ensure coverage, payment policies, regulation of technology to keep up with the pace of innovation.

Like with telehealth, home monitoring equipment has rapidly changed and become an important tool for addressing a range of conditions away from the doctor's office. From diabetes, like Senator Collins was talking about, to heart disease, which you are an expert in. It has also become a popular tool for people to monitor their own health and the health of their children through smart devices like their smartwatches.

If confirmed, what would you do to clarify the regulatory pathways for manufacturers of such devices and products specifically to ensure that they are both consistent, efficient, safe, just make sure they are really doing what they are supposed to and maybe not—maybe helping to promote care, but not in place of care?

Dr. CALIFF. Really appreciate that question, and it is a passion of mine. I mean, cardiology basically goes back to measuring all kinds of things about people and then designing interventions that work, and you made a couple of really, really important points. First, we are seeing this decline in life expectancy that I have already talked about, dominantly in rural America now, and it needs to be dealt with. There aren't going to be enough nurses and doctors to go to every community and provide the care that is needed, so we have got to employ digital technology.

But it also can't be digital technology alone. And I would just put forward this is not the FDA's purview, but I would put forward that the workforce of people needed in the communities to help people interact with digital technology. Now that you all have graciously passed the law that will fund broadband for all of America. That is a great place by which people in rural areas can get employment.

Then, with regard to the regulation, this is a complicated area, and I can assure you that people have not dealt with patients and the issues and health can make really bad mistakes and the use of technology because I haven't seen what happens when the technology is misused, and someone is hurt and badly damaged. And so safety is an issue here, just like everywhere else.

On the other hand, if you are too heavy handed in the regulation, you are impeding a field where essentially, with traditional devices, you make a change and you go all the way back to the manufacturing plant. With software, you just update the code much like we are all used to doing with our iPhones. So there is a spectrum here. There is a Center for Digital Health in the FDA, and Bakul Patel who runs it I have tremendous confidence.

I think, we will have to work across that spectrum. But I would echo more than anything else what you said about, it is a human interface issue, not just a person using the technology, but they are going to need a workforce that can help them use it.

Senator ROSEN. Well, I am glad you brought that up because broadband, of course, I worked on that and the infrastructure bill, and that is really important, and workforce, how do we potentiate the telehealth, all the opportunities we have.

But as you talk about coordination, I know it is not the FDA's purview, but what could you do maybe differently than you might have done in the past, now with, of course, technological changes we have, to improve the coordination between FDA and CMS, and of course Congress to be sure that all of us are moving forward in the same path to provide outcomes that are great for people? It is their health, right. We want positive outcomes.

Dr. CALIFF. I think one of the greatest lessons from my previous time as Commissioner is that it is something I already knew, but you have to experience it to realize we are all just people. And I was reflecting back on Senator Hassan, and I certainly made a number of mistakes, and we have all made mistakes. One of the elements that comes into play here is that the coordination across Federal agencies is a lot more human and complicated than you would think on the outside.

I was surprised to see the defense mechanisms that exist across the Federal Government that we need to break down. And so I very much learned a lot and I really look forward to working with the HHS family and also with Congress to solve these kinds of problems, where we think about the FDA has an essential critical, well-defined role, but if we ran it like a relay race where we just threw the baton down and then the next person had to pick it up and figure out where to go, that doesn't work. And so we do have distinct roles, but those interfaces are absolutely critical.

Senator ROSEN. Yes, I think you are right. We have to work concurrently on all of this instead of maybe consecutively, like you were saying. I see that my time is up. Thank you so much. I will submit the rest of my questions for the record.

Dr. CALIFF. Thank you.

The CHAIR. Thank you.

Senator Marshall.

Senator MARSHALL. Thank you, Madam Chair. Dr. Califf, welcome. And again, thanks for visiting with me one on one, and we appreciate your willingness to put your life out here in front of all of us. Ranking Member, my good friend Senator Burr spoke a little bit earlier about real world evidence.

June of this year, I thought there was enough evidence for boosters that as a prescribing physician myself, I would have recommended it and I did recommend it for my parents and for senior citizens and probably people with health care risk. So in June, I thought there was enough real world evidence, but it was fall by the time the FDA moved on it and really November before my parents were able to get it.

I saw the Delta wave coming. And if we could have got those boosters in senior citizens arms this summer, we would have saved tens and thousands of lives. How can we move more quickly with real world evidence with a drug or vaccine that has already had FDA clearance, but just a new use?

Dr. CALIFF. Well, let's dream a little bit, but I don't think dream is far away if we get the human aspects of this right. There is no

technological limitation now to having immediate access to all of the transactions that are occurring in our health system, the treatments that people get, the conditions that they are diagnosed with, and their outcomes. But we have a labyrinth of information that needs to be knitted together to make that happen so that we have information and as close to real time as possible.

You have seen an approximation of this with the COVID tracker that we all look at every day that shows us almost in real time the number of cases, the hospitalization rates, and the death rates. And so it is very much, if I am confirmed, part of my agenda to get the rules in place, the systems in place, as I have discussed, to give people confidence that it actually is in their interest to share data.

But for that to work, we got to have those rules right and those who misuse people's information need to be severely punished.

Senator MARSHALL. Thank you. If I think about the last 20, 30, 40 greatest miracle drugs that came, have come to fruition in this world, that maybe all of them have a relationship to the United States. What would the international price index, if that was instituted in this country, or Medicare price negotiation, any type of price fixing by the Government, what would that do to innovation in our world of medical—of drugs?

Dr. CALIFF. Well, Senator Marshall, I am not sure we will completely agree on this one but let me just say that I do think that there needs to be, wealthy countries need to share in the cost and in paying their fair share for drugs. I am sure you agree with that. And so, in any kind of negotiation that occurs, if we go too far, it will squelch innovation.

But we are going to find a sweet spot, which I would argue is a little bit off right now because I am acutely aware that, for example, almost a quarter of cancer patients are not following through on the chemotherapy because they don't have the financial means to pay for these effective drugs.

People think of cardiology, my specialty is sort of nuts and bolts, bread and butter. But it turns out financial toxicity is now a significant issue for patients with cardiovascular disease. So I do think we need an adjustment to find the sweet spot, but I also think other countries need to pay their fair share.

Senator MARSHALL. Thank you. RU486 is a drug I have never prescribed as an obstetrician gynecologist, but unfortunately I have had to take care of patients with complications from it, typically in the emergency room. These patients not only have physical complications, hemorrhaging and bleeding, but certain psychological challenges after they have had that abortion.

This kind of remorse afterwards, and I am very troubled by HHS's casual attitude about the prescription—about prescribing RU486. Are you committed that should be in the hands of physicians and prescribers and not handed out like candy?

Dr. CALIFF. Well, as we have already discussed, I think the FDA has to make this decision based on the latest data and the scientific principles. And as we have already discussed also, I know more information is soon to become available. I am not involved in those discussions, but I do trust the FDA staff to make good decisions.

Senator MARSHALL. Okay. I guess I have got time for one more. I was frustrated last year that the FDA moved really quickly on some testing for coronavirus, but not on T cell testing. As a clinician, I just want to have the choice, the ability. I don't want the FDA to decide for me whether I should use the T cell—I just want to know if it is safe, it is available.

What can you do to make sure that the FDA going forward is not choosing winners and losers, and why wouldn't you prioritize the T cell every bit as much as some of the other testing? It just felt like that became a political turmoil rather than trying to do what is best and letting clinicians decide.

Dr. CALIFF. When I came along in the 1970's, cardiology was really exciting, and immunology was this evolving field. It was just amazingly complicated. It was really hard to understand. We have come a long way, and there is no question that T cells—I mean, when you think about it, the B cells now protect us from the acute infection, particularly in the nasal pharynx with the pandemic. The T cells are—that is what is called into effect in the long term to prevent death and hospitalization.

I am totally with you that we need to have T cell testing, but it is also without going into laborious detail, and it is not my area of expertise, I would just say that it is complicated because just measuring something in the blood of someone doesn't give us the information we need because the T cells have a memory.

When they get the right stimulus, they swung into action and created an army of T cells come in and do the job. So I would just say, I know the FDA is interested in this.

I personally think it is a critical issue that we need to continue to work on, but we have to have reliable tests that give us the information we need. And maybe the combination of evolving tests and the real world evidence that we have talked about will give us the information that we need.

Senator MARSHALL. Thank you so much. I yield back.

The CHAIR. Thank you.

Senator Lujan.

Senator LUJAN. Thank you, Chair Murray. Doctor, we have seen a new record high of opioid deaths, with more than 100,000 Americans dying over a 12 month period. In New Mexico, these numbers mean a loss of a loved one from overdose every 14 hours. The FDA has a long track record of proving dangerous opioids without considering public health. A Federal judge presiding over county and state cases against opioid manufacturers and distributors recently wrote, "it is accurate to describe the opioid epidemic as a manmade plague 20 years in the making.

While courts are holding opioid manufacturers and distributors accountable for their actions that caused this epidemic, it is clear that the FDA missed clear signs regarding the risks and benefits of opioids, which created the crisis to take hold."

In response to a question around the role of the FDA about curbing the use of dangerous and addictive prescription drugs, you responded, one of those answers is better prescriber education, which I agree with. The question that I have is, doctor, will you commit to reevaluate the labels?

Dr. CALIFF. Well, Senator, I am committed to do a comprehensive review of the status of opioids early in my tenure, like in the first few months, should I be confirmed. That would include everything, including the labels. Now I would look forward to talking with you about the details of the issues that are involved in doing that, but I am committed to do a comprehensive review of the opioid situation, including the labels.

Senator LUJAN. I think that in your testimony, you also shared that a family member that received a 30 day supply for an acute issue. Had there been more accurate labeling requirements, I don't think that would have happened, in addition to the education. And I think that is one of the important changes that must take place. Another area that I raised when we met personally as well is the FDA convened an advisory committee of scientific experts with a matter of significant public interest, especially as involved, highly controversial or in need of a specific type of expertise.

In 2014 the FDA approved Zohydro, which is a pure hydrocodone drug, despite the FDA Advisory Committee strongly voting against approval in a vote of 11–2 due to the known dangers of overdose and death. It goes back to what that judge said, a crisis 20 years in the making that is manmade.

My question is, as a person that would be in charge of the FDA, if your advisory committee or one of the FDA advisory committees voted overwhelmingly like this, 11–2, on Zohydro, what would you do?

Dr. CALIFF. Well, as I have already said, had the long term studies been done and we had the evidence, I think that decision would have been different. It was not the right decision in the context that it was in. With regard to advisory committees, I think we had a good discussion about this, and I actually went back and looked.

It turns out the FDA makes a decision that is not identical to the advisory committee about 25 percent of the time, but three-quarters of those 25 is for a more stringent reduction in the use of a product instead of more use. So I think when there is an 11–2 vote, the leaders of FDA really need to take a close look and make sure they——

Senator LUJAN. If I can interrupt, I appreciate the evaluation looking at the FDA. I am talking about opioids, and I am talking about constituents that are dying and mistakes that the FDA has made 1 year after another. I am sick and tired of the United States approving one opioid to fix another. It is the dumbest thing that I have—I just, I don't understand it. This is stupid. People are dying because of it.

Heroin, if I may. Heroin didn't get developed out on the streets. It was developed in a lab by a pharmaceutical company. And then here in the United States, we keep approving one after another. Specific to an 11–2 vote on an opioid, doctor, what would you do if you got that vote on something specific to this with Zohydro, and subsequent to that, the FDA approved more without even going to the advisory committee, they just said, oh, we are going to ignore them, and I am going to continue to approve these opioids and kill more people across America. What would you——

Dr. CALIFF. Senator, I wasn't there at that time, but in my leadership role, we instituted a mandatory advisory committee and also

the framework of societal consideration. There are almost no opioids coming through the FDA now for approval. That has really been shut down. And I think the roles that I played were critical in doing that. But I think, I can't argue with your points.

Senator LUJAN. Chair Murray, I have several other questions for the record, especially around non-addictive pain therapies, which I think we need to be doing more about. And I do look forward to following-up on that line of questioning.

There must be more done here in the United States about taking this issue seriously, rather than companies and families making billions of dollars and building empires off the deaths of our constituents and our families. It is just not right, and something has got to change, and I am hoping, doctor, that you can be that person. Thank you, Chair Murray.

Dr. CALIFF. Let me assure you, I am going to—if I am confirmed, I am going to take a very aggressive approach on this and I appreciate your concerns.

The CHAIR. Thank you.

Senator Scott.

Senator SCOTT. Thank you, Madam Chair. And thank you, Dr. Califf, for spending some time with us today talking about some really important issues that we could all spend a day talking about. I only have 5 minutes. Good news for you. So my first question is that you are coming into a very important position in the midst of really headwinds in the public health space. And I appreciate the enormity of your responsibilities, if you are confirmed, to lead the FDA.

How do you view the FDA's role in granting emergency use authorization for the new, as well as repurposed products to address the COVID–19 pandemic? Should the FDA use a wider latitude to ensure multiple avenues, for instance, drugs like by budesonide as well as COVID–19 testing kits, making sure that they are available to combat the pandemic?

Dr. CALIFF. Well, as you know—and thanks, Senator, it is good to be here with a fellow South Carolinian. I am wearing my South Carolina bow tie today that my dad had.

Senator SCOTT. I am just glad it is not Clemson, but continue——

[Laughter.]

Dr. CALIFF. Hey, I am a Clemson man——

Senator SCOTT. I know. I am just joking.

Dr. CALIFF. You are all aware, and it was during my tenure that the EUA guidance was written, that potential benefits need to be weighed against the potential risk. That is authority the FDA is given. And so there is a lot of latitude on the types of things that you mentioned.

Yet I would still point out we need—we do need to have enough evidence that we can make a fair assessment of what the potential is, and we need a system in this country, as I have emphasized over and over, that produces the evidence more quickly.

Because under that framework, it is possible you could get it wrong. There is a, it is different if you have actually measured the benefits and risk and then you are confident about it. And so it is finding that right balance that is really in play for the FDA.

Senator SCOTT. No doubt. I would suggest that based on the severity of the challenge in the public space, that taking the appropriate calculated risks, it seems to be necessary nowadays more than it has been in the past. And I think we can do that in a way that involves coming to good decisions consistently.

On the front, long view of public health, I am excited about the role that the mRNA played in bringing the vaccine to the forefront and saving millions of lives. What is the future of that technology for future needs in the vaccine arena, No. 1?

No. 2, I think about the 7,000 rare blood diseases that have very few therapies, treatments of any sort, and I focus a little bit more on CRISPR technologies for things like sickle cell anemia and that path going forward.

Do you see (A), more application for CRISPR in the rare blood space or blood disease space, and (B), on the future forefront of the mRNAs and vaccines, is that future as bright as it appears it could be with the use of these technologies?

Dr. CALIFF. Well, this is one of the things, Senator, where the excitement of being part of this is what keeps me going and coming back. I mean, I am old enough to remember when the Human Genome Project was just being developed, and now we have the code for the genome, and what you are describing are the downstream consequences of that with reading the code and producing proteins and other substances that determine whether we are sick or healthy. And there are a whole array of technologies specifically with mRNA.

I think it as a platform for vaccines, this is something that we have only dreamed about, but it is a reality now. And this took a collaboration of FDA scientists, and of course, academia and the private sector all working toward a common goal over decades. But you also mentioned CRISPR, and the ability to change the fundamental genome is an amazing possibility, but also has significant risks.

Like everything else, we have got to come up with the ideas, try out, and measure things and see what really works. But almost nothing could be more exciting than curing a rare genetic disease with a gene substitution, perhaps for life.

I think for people with sickle cell disease, I have done a lot of work in NHLBI with Gary Gibbons, who is a great leader there. I think this is something that is really needed, and it ties in, chronic treatment for sickle cell disease, not going so well in this country because many of the patients live off the beaten path of the big high tech centers. And we have got to get treatments that are more effective.

Senator SCOTT. Yes. And, Madam Chair, if you allow 30 seconds.

The CHAIR. Yes, we have several more Senators and votes going so.

Senator SCOTT. Thank you very much. So I would just say that I think we should at least take a second to thank Dr. Francis Collins for his work on the product project that really has produced amazing results for our Nation and frankly for the world, his work—I know he is retiring or just retired. His work has been amazing for all of mankind, No. 1.

No. 2, I would suggest that as we look into that future, the ethical issues around the new technologies like CRISPR will continue to pop up around the world. I know that China has had some challenges already with the use of CRISPR, and so what becomes the solution also becomes a problem. That is called reality. And hopefully will wrestle with those ethical issues in the public forum sometime in the very near future.

The CHAIR. Thank you.

Senator Baldwin.

Senator BALDWIN. Thank you, Chair Murray. I appreciated the chance to visit with you in advance of this hearing, and I wanted to raise an issue that we discussed when we met, the misuse of dairy terms on non-dairy products. It is an ongoing problem, and it is unfair to dairy farmers and processors in Wisconsin and across the country.

The American Academy of Pediatrics has called attention to the misuse of dairy terms because of the potential of these improperly labeled impostors to suggest false nutritional equivalency to milk. I have been working on this issue for years, and I am very glad that the FDA has been moving forward toward providing the industry an updated regulatory guidance.

Dr. Califf, if confirmed, you will have the ability to right this wrong, which is a product, frankly, of FDA's lack of action enforcing its very own rules. Will you commit to finalizing guidance without delay and providing a fair outcome that preserves the use of dairy terms for dairy products and that resolves this matter once and for all?

Dr. CALIFF. Yes, thank you. I mean, there is almost nothing more fundamental about safety than people understanding exactly what they are ingesting, so I am committed to making this a priority, if I am confirmed.

Senator BALDWIN. Thank you. At the beginning of the COVID–19 pandemic, our Nation experienced a critical shortage of donated blood. As one effort to alleviate the shortage, I led many of my colleagues in urging the FDA to update its outdated and discriminatory policies that unnecessarily restrict blood donation by gay and bisexual men. I was pleased to see the agency answer our call and shorten the deferral policy for men who have sex with men from 12 months down to 3 months.

This is certainly a step in the right direction, but any policy that singles out an entire group of people rather than focusing on an individual's personal risk is unscientific and, in my opinion, wrong. We have come a long way in our ability to screen blood and tissue, and the science no longer supports the use of these restrictions. Will you commit to working with me to ensure that the FDA's donor policies are based on individualized risk and not rooted in stigma?

Dr. CALIFF. Short answer is, yes. And I will just point out that I was an intern at University of California, San Francisco when the epidemic started. We didn't know what it was until 3 years into it. And so I understand the origin of this and there were problems with the blood supply at the time.

But we have come a long way with the blood supply, and I am fully aware that there is a study underway to look specifically at

individual risk assessment, and I pledge to bring this home as quickly as we possibly can as this study results come in.

Senator BALDWIN. Thank you. I know the FDA has been working overtime to evaluate a large number of e-cigarette premarket tobacco applications. And I am encouraged that the agency has set a high bar for flavored e-cigarettes to be authorized for sale in the U.S.

But I am concerned by reports that companies are taking advantage of loopholes in the law and switching from making e-cigarettes to making flavored synthetic nicotine products. These products are increasingly popular, and they continue to be targeted to our Nation's children.

As FDA Commissioner, how would you work to address the rise in youth use of synthetic nicotine? And will you commit to working with Congress to ensure that the FDA has the authorities and resources it needs to crack down on these addictive products?

Dr. CALIFF. Yes. And first, let me just say, as Senator Burr pointed out, Mitch Zeller is retiring as head of the Center for Tobacco Products, so appointing the right person in that job is absolutely one of the most important roles at the agency. And second, this is not limited to children. I may have some family members using synthetic nicotine.

I learned as I was going through the paces here, and what people don't realize is that there are two enantiomers of nicotine, one of which is not occurring in nature, that are in this product and its properties are not known. So we have got to close this loophole so that we make sure that we understand the risks and benefits and particularly deal with the issues in children.

Senator BALDWIN. Thank you.

The CHAIR. Thank you.

Senator Hickenlooper.

Senator HICKENLOOPER. Thank you, Madam Chair. And Dr. Califf, thank you for your public service and enjoyed our conversation last week. I hope I wasn't too hard on you. Let me start with a fact that the United States and New Zealand are the only two countries that permit television advertising for pharmaceutical companies. Last year, the industry spent about $4.5 billion on these ads.

I think there are a number of studies that show that the soft music, the glossy scenery does soften and can distort a consumer's ability to carefully evaluate the impact of the drugs. Do you think that the FDA needs to take more active role in ensuring that there is oversight, sufficient oversight in this type of advertising?

Dr. CALIFF. Yes, Senator. First of all, let me just point out I got one Colorado taxpayer sitting behind me here and another payer back home in Colorado couldn't make it to the hearing, so we much appreciate that you are here and——

Senator HICKENLOOPER. Let's forget the questions. We will just go to——

[Laughter.]

Dr. CALIFF. But yes, and I would go beyond that. I mean, I am a doc. And if you, I think if you have docs as this has been done, none of us like the fact that there is advertising of drugs, but we don't make those laws. So the FDA has to regulate it.

I think we need an across the board update and a much more active FDA in terms of getting the right information. It is right there in the mission statement of the FDA to make an understanding of the science behind medical products and their use for the public. And but it is not just advertising done on TV, like you are used to seeing, there is a huge amount of information going on social media that we are going to have to deal with.

As I have talked with 23 of you folks, part of the message is if I am confirmed, I am going to be very aggressive in this area of medical misinformation because one could argue that it is killing more people than any particular disease right now.

Senator HICKENLOOPER. That is very sobering. We talked a little bit about global clinical trials, and we have a number of international partners that are doing critical work around the efficacy of drugs and risk versus benefit. Clearly, we could save money and accelerate getting to the final conclusion on a number of new innovations and new inventions. What can the FDA do to collect data from interconnected clinical trials from our global partners? In other words, what more could the FDA be doing?

Dr. CALIFF. Yes, I am really excited about this. It was in 1988 that I did my first global clinical trial. It was the amazing invention of the fax machine. Actually, this is before the internet was available. Students these days have a hard time actually understanding what that means that there was no internet. And we could enroll 40,000 people in cardiovascular trials in dozens of countries overnight, almost.

We need to get back to that because fundamentally most people want to volunteer for research, if they can do it. And what we have got to do is to use digital technologies to interconnect people better, curate information more effectively.

Much like, as I have mentioned the UK did in COVID with their recovery project, we should build a real of clinical trials very quickly that are representative of the population and get the answers that we need with larger populations.

I think the FDA can lead the way, it needs to work, as we mentioned with Senator Romney in conjunction with CMS, and of course, the NIH.

Senator HICKENLOOPER. Right, absolutely. We are seeing also a crisis now, I think and COVID is only exaggerated what already existed, but as you say, the misinformation that is out there in social media and in the regular media as well around not just prescription drugs per se, but around the FDA's role.

I think there is—we discussed a number of the movie treatments and television episodes around obviously the opioids and the issues there with the Sackler family have been well covered, but it is a larger question of mistrust between FDA employees going in and working for the large pharmaceutical companies and back and forth. How do you go about rebuilding people's trust in the system?

Dr. CALIFF. Well trust once lost is hard to regain. That is an all-time statement, and I think it is true. We are going to have to be much more aggressively outgoing and work on every single aspect of transparency that we can.

Again, if confirmed I do think as a 70 year old person with nothing to gain, I think through most of my career, I have done a pretty good job of calling out other people when they need to contribute.

I mean, a key element to me is that the medical profession and the nursing profession, health systems, we all need to work together to build trust where the evidence is solid and show that we should be trustworthy. It is one thing to say we will have a PR campaign about trust. It is different to show that you are trustworthy.

If confirmed, I would really look forward to working on this because as I said, this may be, we have a lot of great medical therapies now, but if people get the wrong information and don't take advantage of them or take things that don't work or are dangerous, we have really lost the game at that point. Communication is absolutely critical.

Senator HICKENLOOPER. I appreciate your candor. I yield back.

The CHAIR. Thank you.

Senator Burr, any final comments?

Senator BURR. Thank you, Madam Chair. I think we have exhausted all the questions of Committee Members on my side. Let me take this opportunity to publicly congratulate and thank Francis Collins for his leadership at the National Institute of Health. He will be missed and can enjoy retirement. He is a little bit older than you, Rob—can enjoy your retirement——

Dr. CALIFF. If I could, Senator, let me just say, I mean one of the regrets I have if I am confirmed is, I had so much fun working with Francis Collins. He is smart on a lot of areas where I know nothing and I would like to think I contributed something more in the clinical areas to his knowledge, so. But I hear he is going to be in the area still working in his lab, so he will still be available for consults.

Senator BURR. Well, I am sure Francis will make himself available. As it relates to you, I believe you bring a unique skill set at a pivotal time in global innovation. You faced questions on many subjects today, and I think all would agree that you have a daunting job in front of you, if confirmed.

Let me summarize that what we need right now is leadership, leadership that is transparent, leadership that is—displays of trustworthiness by not just people in the industry and in Government, but by consumers, by the American people. I think you are well-prepared to provide that type of leadership.

Madam Chair, I encourage my colleagues to support the nomination of Rob Califf and to do that as expeditiously as we can.

The CHAIR. Thank you very much. And as we end this hearing today, I do want to make clear Mifepristone has a strong track record of safety and effectiveness, and when it comes to women's health, I do expect FDA decision to be made based on science, just as I do all of FDA's decisions.

Dr. Califf, I will be watching closely to make sure decisions are governed by the data, not by politics. And I do ask unanimous consent to submit for the record a study published in the New England Journal of Medicine on the safety of Mifepristone.

[The following information can be found on page 82 in Additional Material:]

The CHAIR. With that, I will end our hearing today. I would like to thank Dr. Califf for joining us and all of our colleagues as well. I look forward to be working with you to make sure FDA continues to uphold the gold standard and put science and data first and keep families across our Country healthy and safe.

For any Senators who wish to ask additional questions, questions for the record will be due Wednesday, December 15th at 5 p.m., and the hearing record will remain open for 10 business days until December 29th for Members who wish to submit additional materials for the record.

With that, the Committee stands adjourned.

ADDITIONAL MATERIAL

AAMC
Association of
American Medical Colleges
655 K Street, NW, Suite 100, Washington, DC 20001-2399
T 202 828 0400
aamc.org

December 13, 2021

The Honorable Patty Murray
Chair
Committee on Health, Education, Labor,
and Pensions
United States Senate
Washington, DC 20510

The Honorable Richard Burr
Ranking Member
Committee on Health, Education, Labor,
and Pensions
United States Senate
Washington, DC 20510

Dear Chairwoman Murray and Ranking Member Burr:

The AAMC (Association of American Medical Colleges) is pleased to support the nomination of Robert M. Califf, MD, as commissioner of the Food and Drug Administration (FDA).

The AAMC is a nonprofit association dedicated to transforming health through medical education, health care, medical research, and community collaborations. Its members are all 155 accredited U.S. and 17 accredited Canadian medical schools; approximately 400 teaching hospitals and health systems, including Department of Veterans Affairs medical centers; and more than 70 academic societies. Through these institutions and organizations, the AAMC leads and serves America's medical schools and teaching hospitals and the millions of individuals employed across academic medicine, including more than 186,000 full-time faculty members, 94,000 medical students, 145,000 resident physicians, and 60,000 graduate students and postdoctoral researchers in the biomedical sciences.

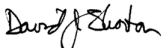
The AAMC strongly believes that Dr. Califf is uniquely qualified to lead the FDA at this critical time. The association and the nation's medical schools and teaching hospitals are proud of our work with the FDA over the years, including throughout the course of the COVID-19 pandemic to identify and advance safe and effective testing, therapeutics, and vaccines. As the virus continues to pose a threat across the country and around the globe, the FDA will continue to play an instrumental role in the nation's response, in addition to its other ongoing, significant work.

Dr. Califf's previous experience as FDA commissioner and as deputy commissioner of the Office of Medical Products and Tobacco will allow a seamless transition to the role and help ensure stability in the midst of the persisting public health emergency. His background as a cardiologist, vice chancellor for clinical and translational research at Duke University, director of the Duke Translational Medicine Institute, and founding director of the Duke Clinical Research Institute also offer him a multi-dimensional perspective on the broad array of stakeholders contributing to and affected by the FDA's work.

Above all else, Dr. Califf's demonstrated commitment to working for the public good is an essential asset in advancing the FDA's mission of protecting the public's health by ensuring the safety and efficacy of the products it regulates.

The AAMC is grateful for your attention and the opportunity to provide these comments in support of Dr. Califf's nomination. Please contact me or AAMC Chief Public Policy Officer Karen Fisher, JD, (kfisher@aamc.org) if you believe the AAMC can be of assistance or provide further information in the confirmation process.

Sincerely,



David J. Skorton, M.D.
President and CEO
Association of American Medical Colleges

National Drug Abuse Treatment
Clinical Trials Network

December 14, 2021

Senator Charles Schumer
Majority Leader
United States Senate
SH-322 Hart Senate Office Building
Washington, DC 20510

Senator Mitch McConnell
Minority Leader
United States Senate
SR-317 Hart Senate Office Building
Washington, DC 20510

Senator Patty Murray
Chair
Senate HELP Committee
United States Senate
154 Russell Senate Office Building
Washington, DC 20510

Senator Richard Burr
Ranking Member
Senate HELP Committee
United States Senate
217 Russell Senate Office Building
Washington DC 20510

To The Senate HELP Committee:

We are a group of clinicians and researchers who work in addiction medicine and are writing to support the approval of the nomination of Robert Califf, MD for the position of Commissioner of the Food and Drug Administration.

We work together in planning and carrying out clinical trials of potential therapeutic advances in the treatment of substance use disorders through a National Institute on Drug Abuse (NIDA) funded consortium known as the National Drug Abuse Treatment Clinical Trials Network (CTN). The CTN is comprised of 16 academic centers partnered with community treatment programs that link treatment providers, patient populations with the addiction research community throughout the country. Much of our work over the past five years has focused on the opioid use disorder epidemic.

Dr. Califf has been involved with the CTN since its inception in 1999. When he was at Duke University, he was instrumental in establishing a CTN site in North Carolina. He made a point of engaging the substance use disorder community with leadership in general medicine to increase the awareness of addictions in the general medical community. He facilitated CTN studies which involved the investigation of substance use disorders in general medical populations. When he initially joined the FDA in 2016, he came to the CTN Steering Committee meeting to discuss opioid use disorder, opioid overdose and intervention strategies with the CTN and NIDA leadership. When he moved to Verily in 2017, he consulted with NIDA leadership about the establishment of treatment for opioid use disorder in primary care offices and advised the CTN leadership about the need to work with big health care data in informing solutions to the opioid epidemic. Dr. Califf has been consistent

National Drug Abuse Treatment
Clinical Trials Network

and active in his interests in addiction treatment and the opioid epidemic. He has advised CTN and NIDA leadership about issues relevant to pharmacotherapy clinical trial design and facilitated work in the area of substance use disorder, in particular opioid use disorders, through his many leadership positions. He has never declined an invitation to consult with the CTN and has sought input from the addiction research community in informing his many efforts in the substance use disorder arena.

We unanimously and heartily support his nomination.

Principal Investigators of the National Drug Abuse Treatment Clinical Trials Network (as signed below)

Kathleen T. Brady, MD, PhD
Distinguished University Professor
Medical University of South Carolina

Lisa A. Marsch, PhD
Andrew G. Wallace Professor
Geisel School of Medicine
Dartmouth College

Adam J. Gordon, MD MPH FACP DFASAM
Elbert F. and Marie Christensen Endowed Research Professorship
Professor of Medicine and Psychiatry
University of Utah School of Medicine

P. Todd Korthuis, MD, MPH
Professor of Medicine and Public Health
Head, Section of Addiction Medicine
Oregon Health & Science University

National Drug Abuse Treatment
Clinical Trials Network

Gail D'Onofrio, MD, MS
Albert E. Kent Professor of Emergency Medicine and Public Health
Yale University School of Medicine

Jennifer Sharpe Potter, PhD, MPH
Vice President for Research (interim)
Professor of Psychiatric and Behavioral Science
University of Texas Health Science Center San Antonio

Niranjan S. Karnik, MD, PhD
The Cynthia Oudejans Harris, MD, Professor of Psychiatry
Associate Dean for Community Behavioral Health, Rush Medical College
Rush University Medical Center

Kimberly Page, Ph.D, MPH, MS
Professor of Internal Medicine
Division of Epidemiology, Biostatistics, and Preventive Medicine
University of New Mexico Health Sciences Center

Roger D. Weiss, MD
Professor of Psychiatry,
Harvard Medical School

Constance Weisner, DrPH, MSW

Professor Emeritus, UCSF
Division of Research, Kaiser Permanente

John Rotrosen, MD
New York University Grossman School of Medicine
NY, NY

Larissa Mooney, MD
Associate Professor of Psychiatry
Director, Addiction Psychiatry Division
Department of Psychiatry and Biobehavioral Sciences
Geffen School of Medicine at UCLA

T. John Winhusen, Ph.D. (he/him)
Donald C. Harrison Endowed Chair in Medicine
Director, Center for Addiction Research
Professor; Vice Chair of Addiction Sciences
Psychiatry and Behavioral Neuroscience Department
University of Cincinnati College of Medicine

Daniel J. Feaster, PhD
Professor of Public Health Sciences
Division of Biostatistics
University of Miami Miller School of Medicine

National Drug Abuse Treatment
Clinical Trials Network

Mary A. Hatch, Ph.D.
Associate Professor
Department of Psychiatry & Behavioral Sciences
Addictions, Drug & Alcohol Unit
University of Washington School of Medicine

José Szapocznik, Ph.D.
Professor, Public Health Sciences, Architecture, Psychology, and Educational & Psychological Studies
Co- Director, Florida Node Alliance, National Drug Abuse Treatment Clinical Trials Network
Chair Emeritus, Department of Public Health Sciences
Founder and Honorary Director, Miami Clinical & Translational Science Institute
University of Miami Miller School of Medicine

December 8, 2021

The Honorable Charles Schumer
Majority Leader
United States Senate
Washington, DC 20510

The Honorable Mitch McConnell
Minority Leader
United States Senate
Washington, DC 20510

The Honorable Patty Murray
Chairwoman, Senate HELP Committee
United States Senate
Washington, DC 20510

The Honorable Richard Burr
Ranking Member, Senate HELP Committee
United States Senate
Washington, DC 20510

Dear Majority Leader Schumer, Minority Leader McConnell, Chair Murray, and Ranking Member Burr,

On behalf of the Academy of Managed Care Pharmacy (AMCP), I submit this letter of support endorsing Dr. Robert Califf, nominated by President Joe Biden to serve as the Commissioner of the Food and Drug Administration (FDA).

AMCP is the professional association leading the way to help patients get the medications they need at a cost they can afford. AMCP's diverse membership of pharmacists, physicians, nurses, biopharmaceutical professionals, and other stakeholders leverage their specialized expertise in clinical evidence and economics to optimize medication benefit design and population health management, while helping patients access safe, cost-effective medications and other therapies. AMCP members improve the lives of nearly 300 million Americans served by private and public health plans, pharmacy benefit management firms, and emerging care models.

With nearly 40 years of experience, Dr. Califf is one of the most respected clinical trial researchers in the country and an internationally recognized expert in cardiovascular medicine. He has led many landmark clinical trials and is one of the most frequently cited authors in biomedical science, with more than 1,200 publications in peer-reviewed literature. Dr. Califf played a pivotal role in the FDA under President Obama, serving as Deputy Commissioner for Medical Products and Tobacco beginning in February 2015 and as FDA Commissioner from February 2016 to January 2017. Prior to joining FDA, Dr. Califf was Vice Chancellor for clinical and translational research at Duke University, director of the Duke Translational Medicine Institute, and founding director of the Duke Clinical Research Institute. He is currently a professor of medicine at the Duke University School of Medicine and Head of Clinical Policy at Verily Life Sciences, a life sciences research organization.

Given Dr. Califf's considerable experience across both the public and private sectors, along with his expertise on health disparities, health outcomes research, and quality of care, AMCP stands ready to

partner with him as FDA Commissioner on increasing patient access to affordable medicines, improving health outcomes, and ensuring health equity for all Americans.

Thank you for the opportunity to support the nomination of Dr. Robert Califf. Given his substantial knowledge and unquestionable qualifications, Dr. Califf is an excellent choice to serve as FDA Commissioner.

Sincerely,

Susan A. Cantrell, RPh, CAE
Chief Executive Officer

December 8, 2021

The Honorable Patty Murray
Chair
U.S. Senate Committee on Health, Education, Labor and Pensions
154 Russell Senate Office Building
Washington, DC 20510

The Honorable Richard Burr
Ranking Member
U.S. Senate Committee on Health, Education, Labor and Pensions
217 Russell Senate Office Building
Washington, DC 20510

Dear Chair Murray and Ranking Member Burr:

The American Pharmacists Association (APhA) strongly supports the swift confirmation of Dr. Robert Califf as Commissioner of the Food and Drug Administration (FDA). APhA is the only organization advancing the entire pharmacy profession. Our expert staff and strong volunteer leadership, including many experienced pharmacists, allow us to deliver vital leadership to help pharmacists, pharmaceutical scientists, student pharmacists, and pharmacy technicians find success and satisfaction in their work, while advocating for changes that benefit them, their patients, and their communities.

Dr. Califf's background as a cardiologist, professor of medicine at Duke University and the founder and director of the Duke Clinical Research Institute, and his commitment to patients position him well to lead the FDA in maintaining the agency's high standards for safety, efficacy, and quality. In addition, Dr. Califf's previous distinguished service as FDA Commissioner and Deputy Commissioner for Medical Products and Tobacco, and commitment to science-based decisions make him uniquely qualified to lead the FDA during this critical time. Dr. Califf's previous FDA tenure enables him to hit the ground running as the agency continues its work to address the COVID-19 pandemic and protect public health.

FDA is responsible for the oversight of more than $2.8 trillion in consumption of food, medical products, and tobacco. Dr. Califf's steadfast leadership is needed at FDA as we come out on the other side of the COVID-19 pandemic and face new challenges in the future. Dr. Califf's experience, knowledge, and understanding, not only of FDA, but also of federal regulatory and legislative processes, clinical research, and medical product development are essential to building on FDA's strengths and carrying out its public health mission.

APhA
American Pharmacists Association

APhA looks forward to continuing to work closely with the FDA under Dr. Califf's leadership to ensure the safety, efficacy, and security of our patients' medications and urges the Senate to confirm his nomination as expeditiously as possible.

Thank you for your consideration of APhA's views.

If you have any questions or need additional information, please feel free to contact Karin Bolte, JD, Director, Health Policy at kbolte@aphanet.org.

Sincerely,

Scott Knoer

Scott Knoer, PharmD, FASHP
Executive Vice President & Chief Executive Officer

December 14, 2021

The Honorable Patty Murray
Chair
Senate HELP Committee
154 Russell Senate Office Building
Washington, DC 20510

The Honorable Richard Burr
Ranking Member
Senate HELP Committee
455 Dirksen Senate Office Building
Washington, DC 20510

Dear Chair Murray and Ranking Member Burr,

We, the undersigned rare disease patient organizations, are writing to enthusiastically endorse President Biden's nomination of Dr. Robert Califf as Commissioner of the Food and Drug Administration (FDA). We ask that the Senate take immediate action to confirm Dr. Califf.

As you know, Dr. Califf joined the FDA in 2015 as the Deputy Commissioner for Medical Products and Tobacco before serving as Commissioner for 11 months starting in February 2016. Prior to joining the FDA, Dr. Califf's career focused on issues that directly impact rare disease patients' lives. As Vice Chancellor of Clinical and Translational Research at Duke University, Dr. Califf led numerous landmark clinical studies in cardiovascular medicine, health outcomes research, health care quality, and clinical research. In addition, he led initiatives to improve clinical research, including the Clinical Trials Transformation Initiative (CTTI), a public-private partnership that included the FDA and Duke.

While interest in rare disease therapy development has increased since the passage of the historic Orphan Drug Act of 1983, the regulatory systems we have in place struggle to meet the unique challenges and complexities inherent in rare disease such as how to design, conduct and analyze clinical trials for small populations. Dr. Califf's previous time as Commissioner and his leadership in the area of innovative clinical trial designs will bring much needed experience to address the unmet needs in the rare disease community.

Most important to us, the undersigned, is that the FDA must continue to expand upon the patient focused drug development momentum, including patient communities and clinical experts as key stakeholders within development and regulatory review. Patients are key partners in all aspects of health, and in all phases of the continuum in therapy and intervention development. Dr. Califf's professional experiences and work with large data initiatives, will enhance the FDA's efforts to identify how best to incorporate patient reported outcomes into the FDA review process.

Dr. Califf's leadership will continue to greatly benefit the more than 30 million Americans with one of the more than 7,000 rare diseases. At an estimated economic cost of $976 billion in

2019[1], we cannot afford to delay the implementation of policy that will help to provide approved therapies for the 93 percent of rare diseases that do not have an approved therapy.

In his work, Dr. Califf continues to advocate for innovative trial design while not sacrificing the use of data to guide the FDA's decision-making process. Dr. Califf's exemplary knowledge of clinical and translational medicine ensures that he will continue to improve the FDA's drug approval process so that patients receive safe and effective treatments at the earliest moment possible.

Sincerely,

American Behcet's Disease Association
Amyloidosis Foundation
Amyloidosis Research Consortium
Angelman Syndrome Foundation
APBD Research Foundation
Autoinflammatory Alliance
Avery's Hope
AXYS
Born a Hero, Research Foundation
CARES Foundation, Inc.
Choroideremia Research Foundation
Cure Sanfilippo Foundation
CureDuchenne
Dana's Angels Research Trust
EB Research Partnership
EveryLife Foundation for Rare Diseases
Foundation for Sarcoidosis Research
Friedreich's Ataxia Research Alliance
Gaucher Community Alliance
Gene Giraffe Project
HCU Network America
Hide and Seek Foundation
Histiocytosis Association
International Foundation for CDKL5 Research
Maryland Rare
Mission: Cure
MitoAction
MLD Foundation
MTS Sickle Cell Foundation, Inc.
Myositis Support and Understanding
National Fragile X Foundation

[1] The National Economic Burden of Rare Disease Study, EveryLife Foundation for Rare Diseases

National Leiomyosarcoma Foundation
National PKU Alliance
NTM Info & Research
Organic Acidemia Association
Parent Project Muscular Dystrophy
People With Empathy
Project Alive
PWSA | USA
Rare New England
SCAD Alliance
Sick Cells
SSADH Association
Stronger Than Sarcoidosis
Syngap Research Fund
Texas Rare Alliance
The Akari Foundation
The Firefly Fund
The Oxalosis and Hyperoxaluria Foundation
The Sudden Arrhythmia Death Syndromes (SADS) Foundation
Undiagnosed Diseases Network Foundation (UDNF)
United Mitochondrial Disease Foundation
USTMA

December 13, 2021

Dear Chairman Murray, Ranking Member Burr, and Members of the US Senate HELP Committee:

As former Commissioners of the Food and Drug Administration (FDA), we are writing to convey our strong support for confirmation of Dr. Rob Califf as Commissioner of Food and Drugs.

We appreciate the Committee's prompt consideration of Dr. Califf's nomination. It is hard to imagine a time when the need for a well-qualified and experienced Commissioner was greater. Thanks in part to timely, science-based, regulatory action by the FDA, the nation has an improving array of tools to fight the COVID-19 pandemic. Yet the emerging omicron variant, the continued evolution of the COVID crisis, and the need for continued advances to address these risks are all reminders of just how critical it is to have a confirmed Commissioner at the helm of the FDA right now. The agency has a dedicated and talented professional staff that has been working intensely on COVID-19 response efforts, and Acting Commissioner Dr. Janet Woodcock has provided invaluable, experienced leadership throughout our public health emergency. But the absence of a confirmed Commissioner complicates the agency's ability to undertake and sustain the leadership needed now to protect and promote the health of all Americans.

Confirming Dr. Califf is critical not only for moving beyond the COVID-19 emergency, but also to help meet FDA's many other major regulatory responsibilities where Senate confirmed leadership is essential for the nation's wellbeing. The FDA regulates up to one-quarter of the U.S. consumer economy, including potentially life-saving therapies, most of the nation's food supply, and tobacco and nicotine products. Confirming Dr. Califf as Commissioner will help ensure that the FDA is well positioned to adapt and respond to these critical public health issues as well.

At this extraordinary time, Dr. Califf has the experience to be effective from day one, having previously served as Commissioner with strong bipartisan support. His public service builds on a lifelong commitment to leadership in promoting public health and advancing clinical science. He has unique experience in leading clinical research as the founder of the renowned Duke Clinical Research Institute and as former Vice Chancellor of Duke University Health System, with over 1,300 academic publications. He has been a lead investigator of many important and impactful clinical trials, resulting in evidence that has helped transform the care of patients with heart attacks and cardiovascular disease as well as many other conditions. His leadership in the original network of the Patient-Centered Outcomes Research Institute (PCORI) advanced the role of collaborative research with direct involvement by patients. As part of his ongoing efforts to improve access to effective therapies to address the nation's opioid crisis, he helped organize the National Institute of Drug Abuse network that conducted key trials showing the effectiveness of medication-assisted therapy for opioid use disorder. As Head of Clinical Policy at Verily Life Sciences, Dr. Califf has helped develop the digital tools that can help us learn

more--and more quickly--about ways to improve the safety and effectiveness of treatments. This includes many efforts to increase the diversity of clinical trials, with more meaningful participation from Americans with different racial and ethnic backgrounds as well as rural Americans.

Many of us have had the privilege of working directly with Dr. Califf on key public health issues. We know that he is deeply committed to public service, to advancing science and clinical evidence, to effective and transparent communication, and to strengthening and modernizing the FDA so that it can address the unprecedented public health challenges and opportunities ahead. We urge you to act now.

Sincerely,

Andrew von Eschenbach, MD

Scott Gottlieb, MD

Stephen Hahn, MD

Margaret Hamburg, MD

Jane Henney, MD

Mark McClellan, MD PhD

NATIONAL HEALTH COUNCIL

National Health Council
1730 M St NW, Suite 500
Washington, DC 20036-4561
(202) 785-3910

December 13, 2021

The Honorable Patty Murray
Chair
Committee on Health, Education, Labor, and Pensions
United States Senate
154 Russell Office Building
Washington, DC 20510

The Honorable Richard Burr
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate
154 Russell Office Building
Washington, DC 20510

Dear Senators Murray and Burr:

The National Health Council (NHC) supports President Joseph Biden's nomination of Robert Califf, MD, as Commissioner of the Food and Drug Administration (FDA) and urges you to confirm him without delay.

Created by and for patient organizations 100 years ago, the National Health Council (NHC) brings diverse organizations together to forge consensus and drive patient-centered health policy. We promote increased access to affordable, high-value, sustainable health care. Made up of more than 140 national health- related organizations and businesses, the NHC's core membership includes the nation's leading patient organizations. Other members include health-related associations and nonprofit organizations including the provider, research, and family caregiver communities; and businesses representing biopharmaceutical, device, diagnostic, generic drug, and payer organizations.

The FDA has weathered one of the most challenging periods in its history. While the existing staff has admirably responded to COVID-19 and other challenges, President Biden's selection of former Commissioner Dr. Califf to head the agency can bring stability and help build on the lessons learned during the pandemic, boosting staff morale, and paving the way for future innovation at a critical time.

Without question, the FDA has accomplished a great deal over the past 18 months, and the current leadership has done an outstanding job navigating this unprecedented time. COVID-19 vaccines, tests, and treatments were thoroughly reviewed and swiftly approved to address the pandemic, a historic accomplishment by all accounts. Despite the pandemic challenges, FDA continued to review and approve numerous treatments for rare and other complex diseases.

A presidential-appointed Commissioner, with all the influence and respect that support from the White House and the Senate bestows, can be a champion for millions of Americans, particularly those with chronic diseases and disabilities. The FDA can be a robust agent for transformational change in our health care ecosystem. As we look to 2022, we also need a Commissioner to guide this evolution with Congress and the agency entering into user fee agreement (UFA) negotiations.

The patient community is proud to have worked with Dr. Califf before, during, and after his time as Commissioner to advance patient engagement at FDA. Under his leadership as Commissioner, patients became active participants in making decisions that will ultimately impact their health. Meaningful patient engagement has led to higher-value products that promote better health outcomes that meet individual's unique needs.

The PDUFA VII commitment letter includes significant continuation of patient-supported priorities that further the science of patient engagement and infuse patient input into a variety of priority areas such as the use of digital health tools in clinical trials, real-world evidence, and the regulation of cell and gene therapies. Given his long-standing championing of patient engagement, we feel strongly he would be a great leader to ensure the UFA implementation will successfully launch or further these important initiatives.

In addition, there are health equity challenges and opportunities at FDA that Dr. Califf is qualified to address. The NHC and our member organizations have redoubled our efforts on finally undoing decades of harm the health care system has caused for marginalized communities by targeting and dismantling health disparities. As part of our work, Dr. Califf has engaged with our members to provide thought leadership on the role FDA and medical product developers can have to address health equity such as greater diversification of clinical trials and patient engagement activities.

As the Senate HELP Committee makes the important decision to confirm the next FDA Commissioner, please consider the voice of people with chronic conditions and disabilities and confirm Dr. Califf.

Please do not hesitate to contact Eric Gascho, Vice President of Policy and Government Affairs if you or your staff would like to discuss these issues in greater detail. He is reachable via e-mail at egascho@nhcouncil.org.

Sincerely,

Randall L. Rutta
Chief Executive Officer

American Heart Association.

December 3, 2021

The Honorable Charles Schumer
Majority Leader
U.S. Senate
Washington, D.C. 20510

The Honorable Mitch McConnell
Minority Leader
U.S. Senate
Washington, D.C. 20510

The Honorable Patty Murray
Chair
Committee on Health, Education, Labor and Pensions
U.S. Senate
Washington, D.C. 20510

The Honorable Richard Burr
Ranking Member
Committee on Health, Education, Labor and Pensions
U.S. Senate
Washington, D.C. 20510

Dear Leader Schumer, Leader McConnell, Chair Murray and Ranking Member Burr:

On behalf of the American Heart Association and its more than 40 million volunteers and supporters, we write to enthusiastically endorse Robert M. Califf, M.D. as President Joseph R. Biden's nominee for Commissioner of the Food and Drug Administration (FDA). We ask that the Senate Health, Education, Labor and Pensions (HELP) Committee and the full Senate vote to confirm Dr. Califf without delay.

The FDA Commissioner serves a central role in addressing critical public health priorities, including ensuring equitable distribution of COVID-19 vaccines, reducing the harm from tobacco products, ensuring food safety and promoting good nutrition, and streamlining the process of drug and device development and review. Dr. Califf's distinguished career in medicine and clinical research, combined with his previous experience as FDA Commissioner, makes him uniquely suited to lead the agency during this especially challenging time in our nation's health.

Dr. Califf's leadership experience has been honed through his prior FDA leadership roles—as the agency's Commissioner, and as its Deputy Commissioner for Medical Products and Tobacco—and as founding director of the Duke Clinical Research Institute. His institutional knowledge of the agency and clinical expertise will allow him to rise to the current public health threats immediately. As a cardiologist, Dr. Califf is particularly patient-centered and understands the agency's central role in improving health. As a researcher, he understands the value of science

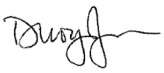
and evidence-based policymaking. As a former public servant, he is an outstanding communicator and recognizes the importance of building trust among diverse individuals and communities. And as a world-renowned thought-leader, he has the strategic vision to modernize and strengthen the agency to meet the public health opportunities and challenges facing the agency and our nation today and tomorrow.

Throughout his career, Dr. Califf has been a relentless force in the fight against heart disease and stroke. He was a lead author of the American Heart Association's 2020 call to action for addressing inequities in rural health, emphasizing the need for innovative approaches to improve rural health to equitably increase healthy life expectancy nationwide. He has also been a driving force behind the American Heart Association's January 2021 commitment to address social determinants of health and the barriers to achieving health equity for all communities—urban, suburban and rural.

Dr. Califf is eminently qualified and ready to lead the FDA. His record demonstrates that he will support the agency's critical efforts to promote public health and reduce the burden of chronic disease. We urge the Senate to act quickly and in a bipartisan manner to confirm Dr. Robert Califf as FDA Commissioner.

Sincerely,

Nancy Brown
Chief Executive Officer
American Heart Association



Donald M. Lloyd-Jones, MD, ScM, FACC, FAHA
President
American Heart Association

cc: Members of the Committee on Health, Education, Labor and Pensions, U.S. Senate

December 13, 2021

Honorable Patty Murray
Chair
Senate Committee on Health, Education, Labor and Pension
Washington, DC 20510

Dear Chairperson Murray,

As the national voice representing the millions of American families whose lives have been upended by the youth vaping epidemic and the predatory behavior of Big Tobacco, Parents Against Vaping E-cigarettes strongly supports the nomination of Dr. Robert Califf to be the Commissioner of the Food and Drug Administration. We commend you on the scheduling of his confirmation hearing and urge the HELP Committee to vote on his nomination, and send it to the Floor for quick consideration by the full Senate.

Dr. Califf has the expertise and the experience to address the numerous important issues currently pending before the FDA. In particular, under Dr. Califf's leadership, we expect the FDA to complete the review of the pending premarket tobacco applications submitted by e-cigarettes companies over 15 months ago, the court ordered deadline of September 9, 2020.

We are optimistic that the FDA will address the issue of the regulation of synthetic nicotine. Companies such as Puff Bar, which in July 2020 was issued a warning the FDA to remove their products from the market for failure to submit pre-market tobacco applications, reemerged claiming that their products, made from synthetic nicotine and being tobacco free, are not subject to regulation by the Center for Tobacco Policy at the FDA. Currently, no entity at the FDA is regulating synthetic nicotine. These unregulated products are available in numerous teen popular flavors, many of which are inexpensive and disposable, will continue to gain popularity and market share. It is time to change this and get these addictive and deceptive products off the market.

In addition, in the coming months, the FDA will be putting forth regulations regarding the elimination the sale of menthol cigarettes. It is imperative to have a leadership in place to ensure these rules and regulations are published in a timely manner.

As a cardiologist, Dr. Califf understands the devastating consequences of tobacco use and how addictive and harmful nicotine is to adolescents' developing brains and lungs. Until all flavored e-cigarettes are removed from the market, we have very little chance of ending the youth vaping epidemic—and, more importantly, keeping younger kids from starting to use dangerous tobacco products in the first place. Now is the time for the FDA to address these issues and end the hold that Big Tobacco has on our children.

We recognize as the end of the year approaches how busy Congress is. We appreciate your leadership in holding Dr. Califf's confirmation hearing a priority for the HELP Committee.

Sincerely,

Dorian Fuhrman and Meredith Berkman
Co-Founders
Parents Against Vaping e-cigarettes (PAVe)

Parents Against Vaping E-cigarettes (PAVe) is a national advocacy and education organization founded by three concerned moms as a grassroots response to the youth vaping epidemic. The catalyst was their discovery in 2018 that a JUUL representative had entered their sons' high-school and, without the school's knowledge,told an assembly of students that JUUL was "totally safe". Powered by volunteers across the country, PAVe advocates at the local, state, and national levels for ending the sale of all flavored e-cigarettes and all menthol and other flavored tobacco products. PAVe also trains parents to educate others in their own communities about the dangers of youth vaping. PAVe's monthly podcast "Big Tobacco Messed with the Wrong Moms" can be heard on all major streaming platforms. www.parentsagainstvaping.org

December 13, 2021

Senator Charles Schumer
Majority Leader
United States Senate
SH-322 Hart Senate Office Building
Washington, D.C. 20510

Senator Mitch McConnell
Minority Leader
United States Senate
SR-317 Hart Senate Office Building
Washington, D.C. 20510

Senator Patty Murray
Chair
Senate HELP Committee
United States Senate
154 Russell Senate Office Building
Washington, D.C. 20510

Senator Richard Burr
Ranking Member
Senate HELP Committee
United States Senate
217 Russell Senate Office Building
Washington, D.C. 20510

RE: Support for Nomination of Dr. Robert Califf as Commissioner of the Food and Drug Administration

Dear Majority Leader Schumer, Minority Leader McConnell, Chair Murray and Ranking Member Burr,

On behalf of the undersigned healthcare organizations –we write to offer our support for Dr. Robert Califf's nomination to serve as Commissioner of the Food and Drug Administration (FDA).

As healthcare providers, we depend on the Food and Drug Administration to ensure the safety and effectiveness of therapies that are the foundation of our ability to care for patients. Senate confirmation of an experienced and highly qualified commissioner is essential to ensure the Agency can carry out this public health mission.

Dr. Robert Califf is a well-qualified candidate who was previously confirmed, with broad bipartisan support, to serve as FDA Commissioner. Dr. Califf brings decades of experience as a world recognized leader in cardiovascular medicine and clinical research. We believe Dr. Califf will bring the leadership needed to advance FDA's work in assuring the safety, efficacy and security of treatments, while helping to speed innovation that supports patient care and public health.

We are honored to support Dr. Califf and thank you for your consideration of his nomination. We encourage the Senate to support our patient care efforts by promptly confirming Dr. Robert Califf as FDA Commissioner. If we can provide any further assistance on this matter, please contact Tom Kraus at tkraus@ashp.org.

Sincerely,

Academy of Managed Care Pharmacy
Alabama Society of Health-system Pharmacists
American Association of Colleges of Pharmacy
American College of Clinical Pharmacy
American College of Rheumatology
American Pharmacists Association
American Society of Consultant Pharmacists
American Society of Health-System Pharmacists
Colegio de Farmaceuticos de Puerto Rico
College of Psychiatric and Neurologic Pharmacists
Florida Society of Health-System Pharmacists
Hematology/Oncology Pharmacy Association
Idaho Society of Health-System Pharmacists
Illinois Council of Health-System Pharmacists
Indiana Society of Health System Pharmacy
Iowa Pharmacy Association
Maryland Society of Health-System Pharmacy
Massachusetts Society of Health System Pharmacists
Michigan Society of Health-system Pharmacists
Mississippi Society of Health System Pharmacists
Missouri Society of Health-System Pharmacists
National Alliance of State Pharmacy Associations
New Mexico Society of Health System Pharmacists
North Dakota Society of Health-System Pharmacists
Ohio Society of Health-System Pharmacists
Pennsylvania Society of Health System Pharmacists
Society of Infectious Diseases Pharmacists
South Carolina Society of Health Systems Pharmacy
South Dakota Society of Health-System Pharmacists
Texas Society of Health System Pharmacists

Senator Charles Schumer
Majority Leader
United States Senate
SH-322 Hart Senate Office Building
Washington, DC 20510

Senator Mitch McConnell
Minority Leader
United States Senate
SR-317 Hart Senate Office Building
Washington, DC 20510

Senator Patty Murray
Chair
Senate HELP Committee
United States Senate
154 Russell Senate Office Building
Washington, DC 20510

Senator Richard Burr
Ranking Member
Senate HELP Committee
United States Senate
217 Russell Senate Office Building
Washington DC 20510

December 1, 2021

Dear Majority Leader Schumer, Minority Leader McConnell, Senator Patty Murray and Senator Richard Burr,

The undersigned organizations, representing millions of patients, advocates, caregivers, and health care providers would like to affirm our support for President Biden's nomination of Dr. Robert Califf as Commissioner of the Food and Drug Administration (FDA). We ask that Senators in the Democratic and Republican caucuses and the Senate HELP Committee vote to confirm Dr. Califf.

The United States is at a pivotal moment in terms of public health. The FDA and patients need the leadership that Dr. Califf will bring as soon as possible and has already proven he can provide to the Agency.

Dr. Robert Califf, President Biden's nominee for FDA Commissioner, is not only well qualified, but has received broad support from both sides of the aisle. As you know, he has already served as FDA Commissioner in 2016 and inspired confidence and praise during his tenure.

We believe Dr. Califf will bring the leadership necessary to the FDA and continue assuring the safety, efficacy and security of treatments while also helping to speed innovation in a new international age for patient safety and public health. With the pandemic still raging, continuation of the FDA COVID-19 response is essential. The next commissioner will have to balance that unprecedented task with a myriad of other priorities, including the reauthorization of the user fee programs, developing a framework for appropriate oversight of tobacco and diagnostic tests and development of post-market data to monitor use of medical products. This task will require a seasoned administrator with knowledge of the agency, which Dr. Califf has.

Dr. Califf brings decades of experience as a world recognized leader in cardiovascular medicine. His in-depth work in clinical research and health outcomes research brings lived experience to the agency that will deeply inform his work. This is a challenging time for the FDA, with many complex and crucial projects under way. We need to confirm a new FDA Commissioner without delay. Dr. Califf has shown that he is a seasoned leader who through his previous professional experience is uniquely positioned to hit the ground running.

We know that Dr. Califf can maximize effectiveness for patients through the FDA. The FDA needs a strong commissioner

with broad support at such a pivotal time and we believe that Dr. Califf's return to the Agency will provide that leadership. Congress must ensure that FDA continues its important mission to provide patients with safe and effective treatments. We ask the Senate to do what is right by patients and immediately confirm Dr. Robert Califf as FDA commissioner.

Sincerely,

AliveAndKickn
Alliance for Aging Research
American Academy of Pediatrics
American Society of Health-System Pharmacists
American Association for Cancer Research
Association of American Cancer Institutes
Barth Syndrome Foundation
Black Women's Health Imperative
CARES Foundation
COPD Foundation
CureHHT
CureSHANK
Cutaneous Lymphoma Foundation.
Dup15q Alliance
EveryLife Foundation for Rare Diseases
Fight Colorectal Cancer
Friedreich's Ataxia Research Alliance
Friends of Cancer Research
Genetic Alliance
GO2 Foundation for Lung Cancer
Grandparents in Action
Hannah's Hope Fund
Hermansky-Pudlak Syndrome Network
ICAN, International Cancer Advocacy Network
Infusion Access Foundation
International Pemphigus and Pemphigoid Foundation
International WAGR Syndrome Association
JDRF
Kids With Heart National Association for Children's
Heart Disorders, Inc.
LUNGevity Foundation
Lupus and Allied Diseases Association, Inc.
Melanoma Research Alliance
Men's Health Network
MLD Foundation
MRSA Survivors Network

National Consumers League
National Infusion Center Association
National Organization for Rare Disorders
NBIA Disorders Association
NTM Info & Research
Parent Project Muscular Dystrophy
Personalized Medicine Coalition
Phelan-McDermid Syndrome Foundation
Prevent Cancer Foundation
Prostate Cancer Foundation
Research!America
SADS Foundation
Solving Kids' Cancer
Susan G. Komen
SYNGAP1 Foundation
The American Heart Association
Tuberous Sclerosis Alliance
U.S. Pain Foundation
US Against Alzheimer's

By Electronic Mail

December 13, 2021

The Honorable Patty Murray
Chair, Committee on Health, Education, Labor and Pensions
United States Senate
154 Russell Senate Office Building
Washington, DC 20510

The Honorable Richard Burr
Ranking Member, Committee on Health, Education, Labor and Pensions
United States Senate
217 Russell Senate Office Building
Washington, DC 20510

Dear Chair Murray and Senator Burr:

The undersigned organizations represent the nation's food and agriculture sector which are an essential part of the economy and are responsible for feeding the nation. Together, our members and their employees are responsible for roughly one-fifth of the country's economic activity, directly supporting nearly 20 million jobs that equals more than 13% of U.S. employment. Americans look to our members to produce the food and beverage staples that they rely on each day to live healthy, fulfilling lives.

On behalf of our sector, we are pleased to see President Biden nominate a highly qualified public health expert in Dr. Robert Califf to lead the U.S. Food and Drug Administration as the next FDA Commissioner. The FDA is one of the most important regulatory agencies within the federal government because it helps ensure the safety, nutritional quality, and security of our nation's food supply.

As you consider the nomination of Dr. Califf and his strong credentials in the medical/public health community, we encourage you and your colleagues to also examine and highlight the importance of a renewed focus at FDA on the food component of FDA's responsibility. During the past 2 years, drug development, public health and vaccine administration – was and had to be - the critical focus of FDA. At the same time, however, most food standards have not been updated in decades even as diets have become more personalized. This area could benefit from additional flexibility to accommodate science-based innovation and changing consumer dietary needs; as well as more expedited ways to finalize pending rules and petitions. We encourage enhanced efforts by FDA to partner with the private sector to foster streamlined processes to advance innovation technology for healthier profile products that can positively impact public health. This partnership with the private sector should also apply to food safety to advance risk-based (vs hazard-based) food safety policies grounded in the best available science.

Another area that could use additional focus is retrospective regulatory impact analyses to determine if food labeling regulations resulted in the type of public health impact they were intended to bring about. These analyses are critical to determining if future regulatory actions are warranted and are a real opportunity and necessity now that the urgency of the public health emergency is stabilizing.

We, the undersigned organizations, value the work of FDA on matters of food safety, food standards, labeling, and nutrition and health. We congratulate Dr. Califf on his nomination and the Committee on moving this nomination forward quickly. We look forward to continuing to work with members of this Committee and the FDA to ensure greater transparency, accountability, and collaboration as we embrace science-based innovations, changing consumer dietary needs and the need for expedited rules and analysis.

Please contact us with any questions. Thank you.

Sincerely,

American Bakers Association
American Frozen Food Institute
American Peanut Council
Consumer Brands Association
Corn Refiners Association
FMI – the Food Industry Association
International Dairy Foods Association
National Confectioners Association
National Fisheries Institute
National Grocers Association
National Restaurant Association
North American Meat Institute
North American Millers' Association
Peanut and Tree Nut Processors Association
SNAC International
United Fresh Produce Association

December 10, 2021

The Honorable Chuck Schumer
Majority Leader
United States Senate
Washington, DC 20510

The Honorable Mitch McConnell
Minority Leader
United States Senate
Washington, DC 20510

The Honorable Patty Murray
HELP Committee Chair
United States Senate
Washington, DC 20510

The Honorable Richard Burr
HELP Committee Ranking Member
United States Senate
Washington, DC 20510

Dear Majority Leader Schumer, Minority Leader McConnell, Chair Murray, and Ranking Member Burr:

On behalf of the physicians and medical students represented by the combined memberships of the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Physicians, we write in support of Dr. Robert Califf's nomination as Commissioner of the Food and Drug Administration (FDA). Dr. Califf is an experienced public health leader with a distinguished career in medicine and research whose previous service at the FDA make him well-qualified to lead the agency. We urge you and your respective caucuses to vote to confirm Dr. Califf without delay.

The members of our organizations provide care to our nation's children, adults, and elderly for a full range of physical, mental and substance use conditions. Each day, our physician members provide health care to patients in communities large and small, urban and rural, rich and poor, and experience firsthand the role that FDA plays in improving the health of the nation. Our members and their patients are impacted each day by products regulated by the agency, including drugs, vaccines, medical and surgical devices, infant formula, food, dietary supplements, cosmetics, and tobacco products. As such, FDA plays a key role in protecting Americans from dangers like food-borne illness, opioid addiction, cigarettes and e-cigarettes, and unsafe medical products and dietary supplements.

Our organizations worked with Dr. Califf during his previous tenure as FDA Commissioner and are confident that he is well suited to respond to the urgent public health needs of today by ensuring the safety, efficacy and of drugs, biological products, and medical devices while also spurring needed innovation. As we come upon the two-year mark of the COVID-19 pandemic, it is crucial that permanent leadership is installed at FDA as soon as possible. Dr. Califf's institutional knowledge and clinical expertise will allow him to immediately address current public health threats and strengthen the agency to respond to future needs.

We stand ready to work with Dr. Califf to ensure Americans have access to safe and effective products. We urge you to immediately confirm Dr. Robert Califf as FDA Commissioner.

Sincerely,

American Academy of Family Physicians
American Academy of Pediatrics
American College of Physicians

Partner Organization Support for Califf as FDA Commissioner

Contents

American Association for Cancer Research

AACR Applauds Nomination of Robert Califf, MD, as FDA Commissioner

PHILADELPHIA — The American Association for Cancer Research (AACR), which consists of more than 49,000 laboratory, translational, and clinical researchers; other health care professionals; population scientists; and patient advocates, strongly supports President Biden's decision to appoint Robert Califf, MD, as Commissioner of the U.S. Food and Drug Administration (FDA).

"While the scientific opportunities that exist today to develop more effective cancer treatments have never been greater, we also recognize that the science is increasingly complex, especially when factoring in the rapidly expanding effectiveness of molecularly targeted therapies and combination therapies," said David A. Tuveson, MD, PhD, FAACR, President of the AACR and Director of the Cold Spring Harbor Laboratory Cancer Center. "Therefore, this extraordinary time of promise requires an experienced and visionary leader at the FDA to ensure that the necessary regulatory framework is in place to approve innovative therapies that are both safe and effective, and Dr. Califf is the right person for this extremely important position. We encourage members of the Senate to move expeditiously to confirm his appointment."

Califf, a renowned cardiologist, is a leading expert on clinical trials. He served as FDA Commissioner, as well as Deputy Commissioner for Medical Products and Tobacco at the FDA during the last couple of years of the Obama administration. Prior to his tenure at the FDA, he was at the Duke University School of Medicine for 30 years where he founded the Duke Clinical Research Institute, one of the largest academic clinical trial operations in the world. Califf is currently senior adviser for Verily, a research organization devoted to the life sciences, and Google Health.

"Dr. Califf's appointment recognizes the vital importance of scientific innovation that is especially needed during this challenging period of the pandemic," said Margaret Foti, PhD, MD (hc), chief executive officer of the AACR. "We are excited about working with Dr. Califf again, along with the talented and innovative individuals at the FDA, to ensure the rapid approval of safe and effective treatments for patients with cancer."

During his previous role at the FDA, the AACR worked closely with Califf. On January 8, 2016, 15 prominent members of the AACR met with him and other senior officials for a day-long meeting to discuss the agency's current thinking on laboratory developed tests, companion diagnostics for cancer therapies, and the regulation of next-generation sequencing-based tests.

Partner Organization Support for Califf as FDA Commissioner

As FDA Commissioner, Califf will also have the benefit of working again with many talented and innovative leaders at the agency, including Richard Pazdur, MD, and his team at the FDA's Oncology Center of Excellence. This impressive team works tirelessly to speed the availability of safe and effective therapies for patients with cancer.

The entire cancer research and patient care community also owes Janet Woodcock, MD, a tremendous amount of gratitude for her extraordinary leadership as FDA Acting Commissioner during the past 10 months and for her vision and steadfast dedication during her impressive 30+ year career at the FDA leading to improvements in the health of all Americans.

American College of Cardiology

Biden Announces Intention to Nominate Robert M. Califf, MD, MACC, as FDA Commissioner

The Biden administration on Nov. 12 announced President Biden's intention to nomination Robert Califf, MD, MACC, as commissioner of the U.S. Food and Drug Administration (FDA). Califf previously served as FDA commissioner from February 2016 through Jan. 20, 2017, during the Obama administration.

Califf "has the experience and expertise to lead the [FDA] during a critical time in our nation's fight to put an end to the coronavirus pandemic," Biden said in a statement. "As the FDA considers many consequential decisions around vaccine approvals and more, it is mission critical that we have a steady, independent hand to guide the FDA. I am confident Dr. Califf will ensure that the FDA continues its science and data drive decision-making," Biden added.

Califf is currently a professor of medicine at the Duke University School of Medicine, where he previously served as vice chancellor of clinical and translational research and founder of the Duke Clinical Research Institute. In addition, he is currently head of clinical policy at Verily Life Science, a life sciences research organization. Previously, Califf was the FDA deputy commissioner for Medical Products and Tobacco.

Read the full White House statement.

"Robert Califf is an acclaimed cardiovascular leader, researcher and clinical trialist in the field of medicine," says ACC President Dipti Itchhaporia, MD, FACC. "As the world of clinical research continues to undergo dramatic shifts, the FDA needs a leader who understands the importance of new drugs, tobacco policy, devices and clinical procedures in improving care and outcomes. A patient-first approach is necessary to address current hot-button issues surrounding efficiency, data collection, digital transformation and inclusivity in clinical trials. Having already led the FDA, we know Dr. Califf would bring a breadth of experience to the role at this critical time in medicine and health care."

Society for Cardiovascular Angiography & Interventions

SCAI Supports Nomination of Robert M. Califf, MD as Commissioner of the FDA

SCAI supports the decision to nominate Robert M. Califf, MD, as Commissioner of the Food and Drug Administration (FDA) stated Dr. Tim Henry, SCAI President, and Dr. Sunil Rao, SCAI's In-coming President.

Partner Organization Support for Califf as FDA Commissioner

Dr. Califf's background as a cardiologist and former FDA commissioner, as well as Deputy Commissioner of the Office of Medical Products and Tobacco, provides critical experience to play a vital role in the nation's continuing COVID-19 public health emergency.

His experience as Vice Chancellor for Clinical and Translational Research at Duke University, director of the Duke Translational Medicine Institute, and founding director of the Duke Clinical Research Institute make him especially qualified to help lead the FDA as it emerges from the current crisis.

Drs. Henry and Rao commented that SCAI and the nation's interventional cardiologists are proud to have worked with Dr. Califf in the past and look forward to continuing to support the FDA regarding COVID-19 issues, medical device review and regulation, and tobacco control matters.

SCAI is a non-profit professional association with over 4,500 members representing the majority of practicing interventional cardiologists and cardiac catheterization teams in the United States, including those providing percutaneous coronary interventions (PCI). SCAI promotes excellence in invasive and interventional cardiovascular medicine through education, and the advancement of quality standards to enhance patient care.

The statement follows President Joe Biden's announcement of his intention to nominate Califf on November 12th.

"As the FDA considers many consequential decisions around vaccine approvals and more, it is mission-critical that we have a steady, independent hand to guide the FDA. I am confident Dr. Califf will ensure that the FDA continues its science and data drive decision-making," Biden stated.

Califf previously served as a FDA commissioner from 2016–17 during the Obama administration and will again face Senate confirmation to assume the role. Janet Woodcock, MD, is currently serving as acting commissioner.

We look forward to working with Dr. Califf and everyone at the FDA to improve the health of people everywhere," Drs. Henry and Rao added.

MULTIPLE MYELOMA Research Foundation

Senator Charles Schumer
Majority Leader
United States Senate
SH-322 Hart Senate Office Building
Washington, DC 20510

Senator Mitch McConnell
Republican Leader
United States Senate
SR-317 Hart Senate Office Building
Washington, DC 20150

Senator Patty Murray
Chair
Senate HELP Committee
United States Senate
154 Russell Senate Office Building
Washington, DC 20510

Senator Richard Burr
Ranking Member
Senate HELP Committee
United States Senate
217 Russell Senate Office Building
Washington, DC 20150

December 1, 2021

Dear Majority Leader Schumer, Republican Leader McConnell, Senator Murray, and Senator Burr,

I'm writing to share my strong support for President Biden's nomination of Dr. Robert Califf as Commissioner of the Food and Drug Administration. I've had the privilege of working closely with Dr. Califf in multiple capacities over the years, and have seen and admired his leadership in action. He is the right person to lead the FDA in this critically important moment for public health, building on his prior service as FDA Commissioner in 2016.

I know you are already familiar with Dr. Califf's extensive CV. I would like to highlight three aspects of his character that bring those sterling qualifications to life.

First is his focus on action and results—something I saw in our work together on President Obama's Precision Medicine Initiative. Dr. Califf's efforts were instrumental in securing a number of advances, from modernizing how the FDA regulates cutting-edge genomic sequencing to using real-world patient experience and evidence to drive faster approvals of new treatments. We need that sense of urgency and accountability today more than ever, with the pandemic still raging and critical health disparities preventing too many Americans from receiving the care they need.

Second is his collaborative orientation. Dr. Califf's own background in medicine, academia, public service, and the private sector has reinforced his understanding of the full and complex health ecosystem, and earned him trust and authority among a wide range of stakeholders. He recognizes the hard work people in varied sectors do each day—from patient advocacy organizations to academic researchers to pharmaceutical companies to policymakers to government entities—to bring life-saving new drugs to market. I see the way his bias toward collaboration has driven success at Verily, where I serve on the advisory board, and I am confident it will only make him more effective as FDA Commissioner.

Third, and crucially, is his deep compassion for patients—informed both by his frontline experience as a physician, and also by his family's own encounters with the U.S. health system. As he has previously testified, his daughter was born with serious congenital heart disease, requiring surgery as an infant. In addition, his late mother had multiple myeloma, a diagnosis I share; and in my capacity as founder of the Multiple Myeloma Research Foundation, I've had many occasions to see the combination of analytical rigor and deep humanity he brings to every conversation about research, trials, treatments, and cures. That combination will serve him—and all Americans—well in his capacity as Commissioner.

In sum, Dr. Robert Califf is the leader the FDA and patients need right now—and for Americans like me who are fighting for our lives, there isn't a moment to waste. I urge you to vote to confirm Dr. Califf without delay.

Sincerely,

Kathy Giusti

Founder
Multiple Myeloma Research Foundation
383 Main Avenue, 5th Fl
Norwalk, CT 06851
Mobile: 203.858.8569
themmrf.org

Co-Chair
Kraft Precision Medicine Accelerator
Harvard Business School

hbs.edu/kraft-accelerator/

SCAI
Society for Cardiovascular Angiography & Interventions

December 14, 2021

Senator Patty Murray
Chair
Senate HELP Committee
SD-428 Dirksen Senate Office Building
Washington, DC 20510-6300

Senator Richard Burr
Ranking Member
SD-428 Dirksen Senate Office Building
Washington, DC 20510-6300

Dear Chair Murray and Ranking Member Burr:

On behalf of The Society for Cardiovascular Angiography and Interventions (SCAI), I am writing to enthusiastically endorse President Biden's nomination of Dr. Robert Califf as Commissioner of the Food and Drug Administration (FDA). We ask that the HELP Committee and the entire Senate take swift and immediate action to confirm Dr. Califf. The United States is at a pivotal moment in terms of public health, and the leadership that Dr. Califf will bring to the FDA is paramount to assuring the public that the safety, effectiveness, and security of human drugs and medical devices remain effective, safe, and affordable during the ongoing public health emergency.

SCAI is a non-profit professional association with over 4,500 members representing the majority of practicing interventional cardiologists and cardiac catheterization teams in the United States, including those providing percutaneous coronary interventions (PCI). SCAI promotes excellence in invasive and interventional cardiovascular medicine through education, and the advancement of quality standards to enhance patient care.

Dr. Califf's career has focused on vital issues that directly impact patients' lives. Dr. Califf successfully fulfilled his tenure as FDA Commissioner from 2016-2017 during the Obama administration. As Vice Chancellor of Clinical and Translational Research at Duke University, Dr. Califf led numerous landmark clinical studies. He became a nationally and internationally recognized expert in cardiovascular medicine, health outcomes research, health care quality, and clinical research. He is one of the nation's leaders in the growing field of translational research – key to making sure advances in science translate into medical care. Dr. Califf also has had vast experience working with FDA. Prior to his appointment to Deputy Commissioner for Medical Products and Tobacco, he served as a member of the FDA Cardiorenal Advisory Panel and FDA Science Board's Subcommittee on Science and Technology. We believe that with Dr. Califf's diverse background, and his exemplary knowledge of clinical and translational medicine, he will continue to improve the FDA's drug approval process while ensuring that patients are receiving the safest and most effective treatments as quickly as possible. We urge his immediate confirmation.

Sincerely,

Tim Henry, MD, MSCAI
President

1400 EYE STREET, N.W. • SUITE 1200 • WASHINGTON, DC 20005
PHONE (202) 296-5469 • FAX (202) 296-5427

December 10, 2021

The Honorable Patty Murray
Chair
Committee on Health, Education, Labor and Pensions
United States Senate
Washington, DC 20510

Dear Chair Murray:

We write to express our strong support for the nomination of Dr. Robert Califf as Commissioner of the of the U.S. Food and Drug Administration. His long and distinguished career as a physician, researcher, and public health leader makes him a superb choice to lead the agency during this challenging time.

Given his past service as Commissioner, Dr. Califf is well prepared to take action from day one to protect our nation's health, including protecting children from tobacco products. If confirmed, his considerable experience and knowledge would help FDA to effectively respond to current challenges, including high levels of youth e-cigarette use and the role that flavors play in attracting kids to tobacco products. In the coming months, FDA will need to complete its review of tobacco product applications for a number of e-cigarettes that are popular with youth and issue a long overdue proposed rule to prohibit menthol cigarettes and flavored cigars. With Dr. Califf's leadership, we are confident that FDA would be able to complete these important tasks in in a timely and evidence-based manner that will benefit public health.

As a cardiologist, Dr. Califf understands the continued devastating impact of tobacco use. Tobacco use has long been the leading preventable cause of death in the U.S. and is responsible for more than 480,000 deaths and an estimated $226 billion in health care costs each year. The harm caused by tobacco is disproportionately borne by certain communities of color, people with lower levels of income and education, people with a behavioral health condition, and LGBT Americans. And e-cigarettes are placing another generation at risk for nicotine addiction and tobacco use.

Dr. Califf would be a strong and effective Commissioner, and we expect that he would use his position to end the youth e-cigarette epidemic and accelerate progress in reducing tobacco use. We urge your Committee to promptly consider and favorably report his nomination to the U.S. Senate and that he be quickly confirmed.

Sincerely,

Matthew L. Myers
President
Campaign for Tobacco-Free Kids

cc: The Honorable Richard Burr, Ranking Member, Committee on Health, Education, Labor and Pensions

Members of the United States Senate Health Committee,

My name is Kristan Hawkins, and I'm the President of Students for Life of America and Students for Life Action. On behalf of our nearly 1,300 active groups and of the more than 127,000 student activists we've trained across the nation, I urge you to strongly scrutinize and oppose the nomination of Dr. Robert Califf to head the Food and Drug Administration.

Dr. Califf previously held this position during the Obama Administration in 2016. Under his leadership, the FDA significantly weakened the health and safety standards, known as Risk Evaluation and Mitigation System (REMS), for Chemical Abortion pills, allowing them to be used as late as 10 weeks in pregnancy, when the pills are less "effective." Additionally, women were no longer required to ingest the Chemical Abortion pills at the abortion facility dispensing the drugs. Instead, women were encouraged to take the drugs at home, essentially acting as an amateur abortionist and DIY-ing their own abortion. The FDA even removed the mandated complication report, leaving the abortion drug distributors accountable for only deaths, not harm.

Now, the FDA is posturing to expand the reckless distribution of Chemical Abortion pills even further. During the COVID-19 pandemic, the abortion industry insisted that abortion access was inhibited, leading to the FDA dropping the REMS completely. This only benefitted Corporate Abortion, making Chemical Abortion more lucrative because of the saved time, money, labor, and other resources. The FDA will announce whether they intend to permanently drop these REMS on December 16th.

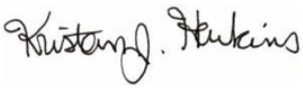
The absence of basic health and safety requirements has allowed abortionists to prescribe dangerous Chemical Abortion pills without examining the woman before or after the abortion, in addition to being absent during the abortion itself. Women are often told to expect bleeding and cramping, sit on the toilet until their deceased baby is expelled from the womb, don't look, and flush. These vulnerable women are abandoned by the abortion industry, left to discern how much pain and bleeding is lethal.

We know that more than 20 women have died after taking the Chemical Abortion pills. Many more have suffered from physical and emotional effects such as fever, immune system inhibition, infection, septic shock, grief, regret, isolation, substance abuse, insomnia, nightmares, depression, anxiety, and even suicidal thoughts. Failure to examine a woman before a Chemical Abortion can also lead to severe issues such as a life-threatening undiagnosed ectopic pregnancy and infertility due to lack of blood type screening.

With nearly 40% of abortions currently being committed using Chemical Abortion pills, this is a major issue that you, our representation on Capitol Hill, must not overlook. Even if you are in favor of abortion, Dr.

Califf's championing of Chemical Abortion without medical oversight – knowing the risks – proves he is motivated by political power, not the safety and wellbeing of the Americans he seeks to serve. Given the opportunity to lead the FDA once again, we fully expect Dr. Califf to continue his abuse of power and act as a radical abortion activist, disregarding the wellbeing of the American people. We strongly urge you to reject this blatantly partisan nomination. The lives of women and their children depend on it.

Sincerely,



Kristan Hawkins
President, Students for Life Action

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Abortion Safety and Use with Normally Prescribed Mifepristone in Canada

Laura Schummers, Sc.D., Elizabeth K. Darling, Ph.D., Sheila Dunn, M.D., Kimberlyn McGrail, Ph.D., Anastasia Gayowsky, M.Sc., Michael R. Law, Ph.D., Tracey-Lea Laba, Ph.D., Janusz Kaczorowski, Ph.D., and Wendy V. Norman, M.D., M.H.Sc.

ABSTRACT

BACKGROUND

In the United States, mifepristone is available for medical abortion (for use with misoprostol) only with Risk Evaluation and Mitigation Strategy (REMS) restrictions, despite an absence of evidence to support such restrictions. Mifepristone has been available in Canada with a normal prescription since November 2017.

METHODS

Using population-based administrative data from Ontario, Canada, we examined abortion use, safety, and effectiveness using an interrupted time-series analysis comparing trends in incidence before mifepristone was available (January 2012 through December 2016) with trends after its availability without restrictions (November 7, 2017, through March 15, 2020).

RESULTS

A total of 195,183 abortions were performed before mifepristone was available and 84,032 after its availability without restrictions. After the availability of mifepristone with a normal prescription, the abortion rate continued to decline, although more slowly than was expected on the basis of trends before mifepristone had been available (adjusted risk difference in time-series analysis, 1.2 per 1000 female residents between 15 and 49 years of age; 95% confidence interval [CI], 1.1 to 1.4), whereas the percentage of abortions provided as medical procedures increased from 2.2% to 31.4% (adjusted risk difference, 28.8 percentage points; 95% CI, 28.0 to 29.7). There were no material changes between the period before mifepristone was available and the nonrestricted period in the incidence of severe adverse events (0.03% vs. 0.04%; adjusted risk difference, 0.01 percentage points; 95% CI, −0.06 to 0.03), complications (0.74% vs. 0.69%; adjusted risk difference, 0.06 percentage points; 95% CI, −0.07 to 0.18), or ectopic pregnancy detected after abortion (0.15% vs. 0.22%; adjusted risk difference, −0.03 percentage points; 95% CI, −0.19 to 0.09). There was a small increase in ongoing intrauterine pregnancy continuing to delivery (adjusted risk difference, 0.08%; 95% CI, 0.04 to 0.10).

CONCLUSIONS

After mifepristone became available as a normal prescription, the abortion rate remained relatively stable, the proportion of abortions provided by medication increased rapidly, and adverse events and complications remained stable, as compared with the period when mifepristone was unavailable. (Funded by the Canadian Institutes of Health Research and the Women's Health Research Institute.)

From the Department of Family Practice (L.S., W.V.N.) and the Centre for Health Services and Policy Research, School of Population and Public Health (K.M., M.R.L.), University of British Columbia, Vancouver, ICES (L.S., E.K.D., A.G.) and the Department of Obstetrics and Gynecology (E.K.D.), McMaster University, Hamilton, ON, the Department of Family and Community Medicine, University of Toronto, and the Women's College Research Institute, Women's College Hospital, Toronto (S.D.), and the Department of Family and Emergency Medicine, University of Montreal, Montreal (J.K.) — all in Canada; the Centre for Health Economics Research and Evaluation, University of Technology, Sydney (T.-L.L.); and the Department of Public Health, Environments, and Society, Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London (W.V.N.). Dr. Norman can be contacted at wendy.norman@ubc.ca or at the Department of Family Practice, University of British Columbia, 5950 University Blvd., Vancouver, BC, V6T 1Z3, Canada.

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Access to safe abortion is a human right and a key component of reproductive health, yet inadequate access remains a global concern.[1] A medical abortion regimen of mifepristone and misoprostol has been shown to be safe.[2-4] Mifepristone is approved for use in the United States with Risk Evaluation and Mitigation Strategy (REMS) restrictions[5] (including mandatory prescriber certification, observed dosing, dispensing by the prescriber or medical facility with the exclusion of pharmacies, and submission of a prespecified patient consent form) and elsewhere with similar restricted approvals.[6,7] Professional organizations have called for the removal of REMS restrictions because they impede access to abortion services without improving safety.[8] However, high-quality data with respect to abortion safety and effectiveness when mifepristone is available without REMS-like restrictions are lacking.[9]

Mifepristone was first marketed in Canada in January 2017 as a 200-mg tablet combined with 800 μg of misoprostol.[10] Approval came more than 15 years after approval in the United States and more than 25 years after similar rulings in France, Sweden, and the United Kingdom.[11] Initially, regulatory restrictions in Canada were similar to REMS restrictions.[12] By November 7, 2017, Canadian regulators had removed these restrictions so that mifepristone could be prescribed and dispensed as a normal prescription medication and had expanded approved use from 49 to 63 days after the patient's last menstrual period.[13] This action resulted in a globally unprecedented practice of permitting any physician or nurse practitioner to prescribe, any pharmacist to dispense, and patients to independently administer mifepristone when, where, and if they chose.[14] Before 2017, medically induced abortions made up only 4% of all abortions in Canada and used off-label regimens of misoprostol with or without methotrexate. These regimens have reduced effectiveness (84 to 97%) and a high risk of teratogenicity if the abortion fails.[4,15]

We compared abortion use, safety, and effectiveness during the period after mifepristone had become available without REMS-like restrictions with the period before mifepristone had been available in Ontario, Canada (representing nearly 40% of the Canadian population).

METHODS

DATA SET

In Canada, universal single-payer health care — including coverage for abortion services and management of its complications — is provided by each province or territory. We used linked administrative health data[16] to create a population-based cohort of all female Ontario residents between the ages of 12 and 49 years who had received abortion services from January 1, 2012, to March 15, 2020. We linked records from practitioner visits, all hospital visits, and outpatient prescriptions using a secure data platform at ICES (formerly known as the Institute for Clinical Evaluative Sciences) at McMaster University.[16,17] We excluded events that had occurred within 6 weeks before or after a missed abortion (pregnancy loss without expulsion) or spontaneous abortion (pregnancy loss with expulsion) and those occurring within 6 weeks after delivery at 25 weeks or more of gestation to avoid including procedures that could have been misclassified as abortions. Details regarding the data set are provided in Figure S1 and Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org. Ethics approval for the study was granted by the University of British Columbia.

EXPOSURE AND OUTCOMES

The exposure we examined was the regulatory change that made mifepristone available as a normal prescription. Outcomes included measures of abortion use, safety, and effectiveness.

We evaluated outcomes regarding abortion use that included the abortion rate, which was calculated according to the international standard as the annual number of abortions among female residents between 15 and 49 years of age per 1000 female residents in that age group,[18] the percentage of all abortions that were medically induced, and the percentage of all abortions that were provided at 14 weeks or more of gestation (second-trimester abortion). (In the calculation of the abortion rate, the lower age for female residents was 15 years, as compared with a lower age of 12 years that was used for all other calculations in our study cohort.) Abortion safety outcomes within 6 weeks after abortion were severe adverse

events, including any blood transfusion, abdominal surgery (laparotomy, laparoscopy, or hysterectomy), admission to an intensive care unit, or sepsis that occurred during a hospitalization associated with an abortion-complication code. Complications of abortion included genital tract or pelvic infection, hemorrhage (delayed or excessive bleeding that complicated complete or incomplete abortion), embolism, shock, renal failure, damage to pelvic organs or tissues (including uterine perforation), venous complications, and other or unspecified complications. Outcomes regarding abortion effectiveness were the incidence of subsequent uterine evacuation (aspiration after medical abortion, reaspiration after surgical abortion, or subsequent abortion procedure), ongoing intrauterine pregnancy continuing until delivery, and ectopic pregnancy diagnosed within 6 weeks after the abortion date. Detailed outcome definitions are provided in Table S1.

STATISTICAL ANALYSIS

We tabulated the incidence of each outcome according to the mifepristone regulatory period. We then conducted interrupted time-series analysis using segmented generalized mixed-effects regression to compare the expected incidence and trend for each outcome based on the period before mifepristone had become available with the observed level and trend after the availability of mifepristone with a normal prescription. We used log binomial regression to model incidence outcomes and Poisson regression with population offset to calculate the abortion rate; models were adjusted for outcome trends before the approval of mifepristone and accounted for autocorrelation and correlated residuals (File 1 in the Supplementary Appendix).[19,20] We used 6-month moving averages to smooth the resulting estimates. We examined outcomes from January 1, 2017, through November 6, 2017, descriptively but excluded this period from our models because it included rapid, incremental regulatory changes.[13]

We graphed the observed and expected monthly outcome incidence (quarterly for outcomes with <6 events in any month) following best practices.[21] We estimated risk differences and risk ratios for each outcome by comparing the observed with expected values for September 2019, a time point selected a priori to balance model stability (greatest in the middle of the study period) and integration of mifepristone into practice (greatest at the end of the study period). We used bootstrapping with 200 samples drawn with replacement to estimate 95% confidence intervals[22] without adjustment for multiple comparisons. All analyses were conducted with the use of SAS software, version 7.51, and R software (code in File 2 in the Supplementary Appendix).

To examine the robustness of our findings to modeling specification, we conducted sensitivity analyses using segmented generalized least-squares regression, with autocorrelation terms selected on the basis of the Durbin–Watson test[23-25] and visual examination of autocorrelation function and partial autocorrelation function residuals.[25] We conducted subgroup analyses that were restricted to first-trimester abortions and then further restricted to first-trimester medical abortions.

RESULTS

CHARACTERISTICS OF THE STUDY POPULATION

Of the 314,859 induced abortions in Ontario, Canada, from January 1, 2012, through March 15, 2020, the majority (89.3%) were surgical (with 94.6% performed by means of suction aspiration), approximately 10% were medical abortions, and less than 0.1% were unclassified. Table 1 shows cohort characteristics according to the regulatory period for mifepristone.

DESCRIPTIVE ANALYSES OF ABORTION OUTCOMES

The abortion rate per 1000 female residents of reproductive age and the incidence of all other outcomes are presented descriptively according to the regulatory period in Table 2. (Components of the composite outcomes are shown in Table S2.) The abortion rate decreased from 11.9 abortions per 1000 female residents between the ages of 15 and 49 years of age before mifepristone had become available to 11.3 per 1000 female residents after mifepristone had become available with a normal prescription. The percentage of all abortions that were provided medically increased from 2.2% before mifepristone had become available to 8.3% while mifepristone was restricted and then to 31.4% after mifepristone had become available with a normal prescription. The rate of second-trimester abortions declined from 5.5% of all abortions to 5.1% after the availability of mifepristone with a normal prescription.

Table 1. Characteristics of Patients Undergoing Medical or Surgical Abortion, According to Period of Availability of Mifepristone.

Characteristic	Mifepristone Not Available (N=195,183)	Mifepristone Available with Restrictions (N=35,644)	Mifepristone Available without Restrictions (N=84,032)
	January 2012–December 2016	January 1, 2017–November 6, 2017	November 7, 2017–March 15, 2020
		number of patients (percent)	
Age — yr*			
<20	20,034 (10.3)	2,969 (8.3)	6,643 (7.9)
20–24	54,346 (27.8)	9,208 (25.8)	20,247 (24.1)
25–29	47,598 (24.4)	8,909 (25.0)	21,717 (25.8)
30–34	36,640 (18.8)	7,369 (20.7)	17,838 (21.2)
≥35	36,565 (18.7)	7,189 (20.2)	17,587 (20.9)
Nulliparous	104,824 (53.7)	19,030 (53.4)	45,902 (54.6)
Neighborhood income†			
Lowest quintile	55,076 (28.2)	9,737 (27.3)	22,360 (26.6)
Highest quintile	24,852 (12.7)	4,603 (12.9)	11,075 (13.2)
Neighborhood ethnic concentration‡			
Highest quintile	82,143 (42.1)	14,627 (41.0)	33,600 (40.0)
Lowest quintile	19,424 (10.0)	3,552 (10.0)	8,451 (10.1)
Rural residence§	11,709 (6.0)	2,174 (6.1)	5,195 (6.2)

* Trends regarding the patient's age at which abortion was performed in Ontario continued a historic gradual and steady increase over the study period, which was consistent with an increase in age in the population-based trends during this period.

† The neighborhood income quintile was drawn from the Registered Persons Database file from the Institute for Clinical Evaluative Sciences and was defined on the basis of the Nearest Census-Based Neighborhood Income Quintile from Census Canada.

‡ The neighborhood ethnic concentration, which is part of the Ontario Marginalization Index,[26] refers to high area-level percentages of recent immigrants and persons belonging to a "visible minority" group, which was defined by Statistics Canada as "persons, other than aboriginal peoples, who are non-Caucasian in race or non-white in color." The highest concentration of such residents is the top quintile, and the lowest concentration is the lowest quintile.

§ Rural residence is defined as all territory lying outside population centers.

Abortion safety outcomes remained stable during the period before mifepristone had become available and during the period after its availability with a normal prescription (severe adverse events, 0.03% and 0.04%, respectively; and abortion complications, 0.67% and 0.74%, respectively). Subsequent uterine evacuation increased from 1.0% to 2.2%, and ongoing intrauterine pregnancy continuing until delivery increased from 0.03% to 0.08%. Ectopic pregnancy that was detected after abortion increased from 0.15% to 0.22%.

TIME-SERIES ANALYSES OF ABORTION OUTCOMES

Interrupted time-series graphs of abortion-use outcomes are presented in Figure 1, abortion safety outcomes in Figure 2, and abortion-effectiveness outcomes in Figure 3. Adjusted risk differences and risk ratios from these models comparing the period before mifepristone had become available with the nonrestricted period are presented in Table 2.

During the study period, the abortion rate continued an absolute decline, although as compared with the trend before the approval of mifepristone, we noted an increase of 1.2 abortions per 1000 female residents (95% confidence interval [CI], 1.1 to 1.4) over the predicted rate. The proportion of all abortions that were medical increased by an adjusted risk difference of 28.8 percentage points (95% CI, 28.0 to 29.7).

Table 2. Safety and Effectiveness of 314,859 Abortions Provided during the Study Period.*

Outcome	Mifepristone Not Available (N = 195,183)	Mifepristone Available with Restrictions (N = 35,644)	Mifepristone Available without Restrictions (N = 84,032)	Adjusted Risk Difference (95% CI)††	Adjusted Risk Ratio (95% CI)
	January 2012–December 2016	January 1, 2017–November 6, 2017	November 7, 2017–March 15, 2020		
Abortions provided					
No. of female residents in age cohort	3,268,428	3,272,448	3,312,061		
Annual rate of abortion per 1000 female residents in age cohort‡	11.9	10.9	11.3	1.2 (1.1 to 1.4)	1.1 (1.1 to 1.2)
Type of abortion — no. (%)					
Medical abortion	4,307 (2.2)	2,962 (8.3)	26,434 (31.4)	28.8 (28.0 to 29.7)	5.3 (4.7 to 5.9)
Second-trimester abortion at ≥14 wk of gestation	10,830 (5.5)	2,072 (5.8)	4,300 (5.1)	−0.22 (−0.63 to 0.19)	0.96 (0.88 to 1.04)
Abortion safety — no. (%)					
Severe adverse events§	53 (0.03)	9 (0.03)	29 (0.04)	0.01 (−0.06 to 0.03)	1.2 (0.4 to 3.4)
Complications¶	1,434 (0.74)	239 (0.67)	578 (0.69)	0.06 (−0.07 to 0.18)	1.1 (0.9 to 1.3)
Ongoing pregnancy — no. (%)					
Subsequent uterine evacuation‖	2,029 (1.0)	518 (1.5)	1,882 (2.2)	1.1 (0.9 to 1.3)	2.0 (1.7 to 2.3)
Ongoing pregnancy continuing until delivery	51 (0.03)	15 (0.04)	70 (0.08)	0.08 (0.04 to 0.10)	7.8 (2.2 to 33.6)
Ectopic pregnancy detected after abortion	289 (0.15)	57 (0.16)	182 (0.22)	−0.03 (−0.19 to 0.09)	0.88 (0.54 to 1.40)

* Adjusted risk differences and risk ratios are for the period after mifepristone was available without restrictions as compared with the period before mifepristone was available. The calculations were performed by means of interrupted time-series segmented regression analyses among all surgical and medical abortions after adjustment for outcome trends during the period before mifepristone had been available. CI denotes confidence interval.

† The adjusted risk difference is shown in percentage points for all categories except for the abortion rate per 1000 female residents.

‡ The annual abortion rate was calculated as the number of abortions provided among female residents between the ages of 15 and 49 years per 1000 female residents in the same age cohort in the population per year.

§ Severe adverse events included blood transfusion, abdominal surgery (laparotomy, laparoscopy, and hysterectomy), admission to an intensive care unit, or sepsis, all concurrent with an abortion complication. A detailed definition is provided in Table S1 in the Supplementary Appendix.

¶ Abortion complications included incomplete or complete abortion complicated by infection, hemorrhage, embolism, damage to pelvic organs, venous complications, or other complications after an induced abortion.

‖ Subsequent uterine evacuation included aspiration, reaspiration, or subsequent abortion procedure in the same pregnancy.

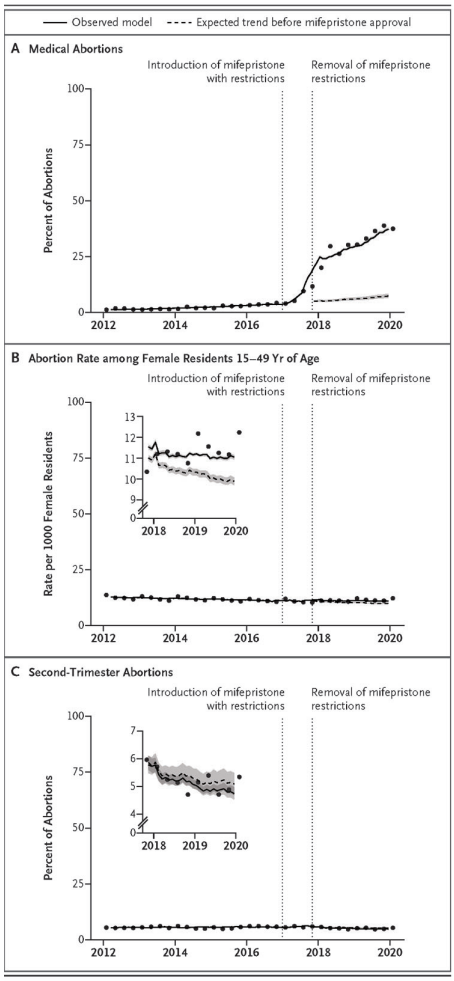

Figure 1. Changes in the Percentages of Medical and Second-Trimester Abortions among All Abortions and in Abortion Rates.

Shown are the results of interrupted time-series analyses of the level and trend of abortion outcomes in Ontario, Canada, among all surgical and medical abortions that were provided before the introduction of mifepristone in the province (2012 through 2016), after the introduction but with Risk Evaluation and Mitigation Strategy (REMS)–like restrictions (January 1, 2017, through November 6, 2017), and after a regulatory change to remove restrictions, which made mifepristone available by normal prescription (November 7, 2017, through March 15, 2020). Panel A shows the percentage of all abortions that were performed medically at any gestational age. Panel B shows the annual abortion rate among female residents between the ages of 15 and 49 years per 1000 female residents in the same age group in the population. Panel C shows the percentage of second-trimester abortions (≥14 weeks of gestation) among all abortions. In Panels B and C, the insets show the same data on an expanded y axis; shading indicates 95% confidence intervals. The expected outcomes if mifepristone had not been available were estimated from segmented mixed-effects models (log binomial regression in Panels A and C and Poisson regression with population offset in Panel B) and smoothed with the use of a 6-month moving-average function.

The rate of second-trimester abortions showed a stable, continuous decline (adjusted risk difference, −0.22 percentage points; 95% CI, −0.63 to 0.19). Abortion safety outcomes were materially stable, with an adjusted risk difference of 0.01 percentage points (95% CI, −0.06 to 0.03) for severe adverse events and 0.06 percentage points (95% CI, −0.07 to 0.18) for complications. The rate of subsequent uterine evacuation increased modestly, with an adjusted risk difference of 1.1 percentage points (95% CI, 0.91 to 1.3), and the rate of ongoing intrauterine pregnancy that continued until delivery increased by 0.08 percentage points (95% CI, 0.04 to 0.10). The rate of ectopic pregnancy that was detected after abortion was materially stable, with an adjusted risk difference of −0.03 percentage points (95% CI, −0.19 to 0.09).

Interrupted time-series graphs from generalized least-squares regression with the use of aggregated monthly data showed the robustness of the findings to modeling specification (Figs.

S2, S3, and S4). Changes in outcome incidences and trends after mifepristone availability with a normal prescription were consistent for all outcomes except for the percentage of second-trimester abortions, for which aggregated models indicated a slight reduction (−0.92 percentage points; 95% CI, −1.40 to −0.48).

OUTCOMES AFTER FIRST-TRIMESTER ABORTION

Outcome incidences among all first-trimester abortions are presented in Tables S3 and S4 and Figures S5, S6, and S7; outcomes among first-trimester medical abortions are provided in Tables S5 and S6. The percentage of first-trimester abortions that were performed medically increased from 1.6% before mifepristone was available to 32.4% after mifepristone was available without restrictions. Severe adverse events were rare among first-trimester medical abortions (<6 events per 25,744 abortions [too infrequent to report exact incidence]), the incidence of abortion complications was 0.76%, and the incidence of subsequent uterine evacuation was 4.5%. Similarly, ongoing intrauterine pregnancy was uncommon, with 0.13% continuing to delivery. Ectopic pregnancy detected after abortion that occurred with any severe adverse event was also rare (<6 per 314,859 abortions).

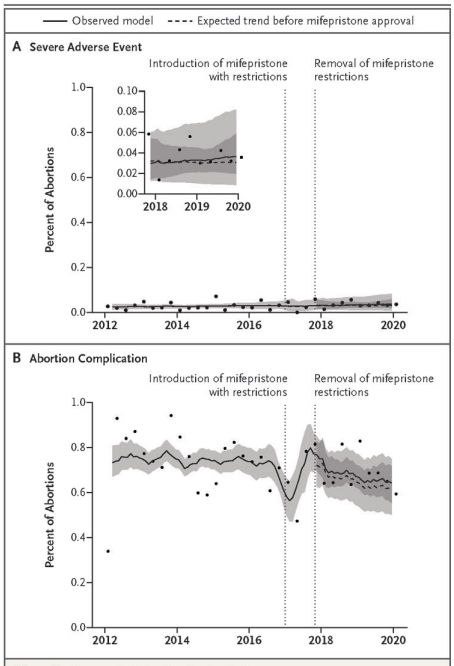

Figure 2. Changes in Abortion Safety Outcomes.

Shown are the results of interrupted time-series analyses of the level and trend of abortion safety in Ontario, Canada, among all surgical and medical abortions provided during the study period. Panel A shows the incidence of severe adverse events, which included any blood transfusion, abdominal surgery (laparotomy, laparoscopy, or hysterectomy), admission to an intensive care unit, or sepsis that occurred during a hospitalization associated with an abortion-complication code. Panel B shows abortion complications, which included genital tract or pelvic infection, hemorrhage, embolism, shock, renal failure, damage to pelvic organs or tissues, venous complications, and other or unspecified abortion complications. In Panel A, the inset shows the same data on an expanded y axis; shading indicates 95% confidence intervals.

DISCUSSION

We comprehensively examined changes in abortion use, safety, and effectiveness during the period when mifepristone had become available without REMS-like restrictions in a population-based cohort of abortion service users in Ontario, Canada. We found that after mifepristone had become available with a normal prescription dispensed by pharmacists and taken at user discretion, abortion rates were materially stable, medical abortion uptake was rapid, and abortion-related adverse events and ectopic pregnancy remained rare, as compared with before mifepristone had been available.

The modestly slower decline in the abortion rate, relative to the expected decline based on the trend before mifepristone had become available, may be due in part to the provision of abortion earlier in pregnancy. Since 4 to 7% of pregnancies per week in the first trimester[27] end in spontaneous abortion, the availability of abortion at earlier gestational ages would increase the abortion rate by enabling termination of pregnancy before the occurrence of miscarriage, even in the absence of a true increase in demand for abortion. The availability of mifepristone without restrictions may have slowed the decline in the abortion rate through improved abortion access, a

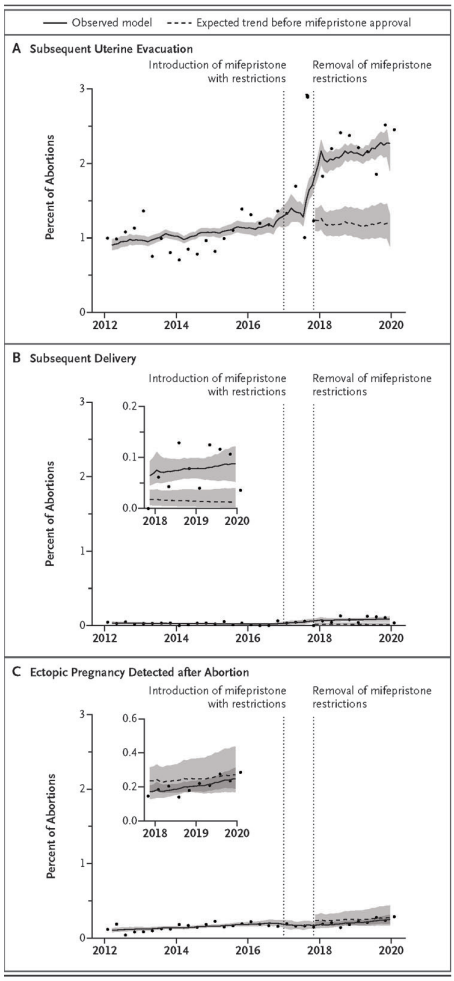

Figure 3. Abortion Effectiveness and Ongoing Pregnancy Outcomes.

Shown are the results of interrupted time-series analyses of the level and trend of ongoing pregnancy outcomes among all surgical and medical abortions provided during the study period. These outcomes include the incidences of uterine evacuation after abortion (Panel A), ongoing intrauterine pregnancy continuing until delivery (Panel B), and ectopic pregnancy detected after abortion (Panel C). Shading indicates 95% confidence intervals.

hypothesis that is consistent with findings that restrictive policies regarding the prescription of mifepristone worsen access to abortion[28] and that abortion rates increase when access improves.[29] Because we did not measure pregnancy intention in our study, we cannot differentiate trend changes in unintended pregnancy from changes in the fraction of pregnancies that were terminated. Our findings indicate that improved abortion access was not associated with a material increase in the abortion rate.

The uptake of mifepristone for medical abortion under Canada's unrestricted regulations was faster than reported in settings with restrictive regulations. Although more than one third of abortions in Ontario were medically induced 2 years after mifepristone had been available as a normal prescription, 5.2% of abortions in the United States were medically induced 2 years after mifepristone availability, with the percentage slowly increasing to 39.0% 17 years after availability.[2] Similarly slower uptake has been reported in European settings that have mifepristone restrictions, even among those where mifepristone had been introduced long after best practice guidelines had been established.[30]

Our findings indicate that abortion remained safe and ongoing pregnancy remained infrequent after unrestricted access to mifepristone. Without observed administration, some patients with a prescription for mifepristone may have never used it.[9] However, the infrequent occurrence of ongoing intrauterine pregnancy indicates that patients who received mifepristone most often correctly used the medication without supervision.[31] Our abortion safety and effectiveness findings are consistent with the results

of recent studies examining patient-reported outcomes during the coronavirus disease 2019 pandemic, when REMS-like restrictions were temporarily removed in some settings.[9,32,33] A study involving 52,142 patients in the United Kingdom showed no material differences in success rates or serious adverse events between abortions provided under REMS-like restrictions and a telemedicine-hybrid model with investigations such as ultrasonography performed only when indicated.[33]

The small increase in the incidence of ectopic pregnancy that was detected after unrestricted access to mifepristone was consistent with the increasing trend before the availability of mifepristone, which indicated no increase over the expected incidence. A 2012 cross-sectional survey of abortion providers in the United States and Canada showed that more than 90% of providers routinely performed ultrasonography before abortion,[34] even though the value of such imaging in the absence of known ectopic risks or symptoms had not been shown.[2,35] Ectopic pregnancy is more likely to be detected after abortion that is provided at earlier stages of gestation before a clinical or ultrasonographic diagnosis. Because undiagnosed ectopic pregnancy can lead to tubal rupture and death,[36] identifying ectopic pregnancy before the onset of complications with the use of clear clinical protocols[2,4] is essential, although such procedures do not need to be performed before the initiation of medical abortion.[33]

Our safety and ongoing pregnancy findings among first-trimester medical abortions during the period after unrestricted access to mifepristone were consistent with reports from other settings with restricted access.[2,4] In settings with REMS-like restrictions, first-trimester medical abortions resulted in major adverse events in 0.3 to 0.5% of women[2,4,31] and blood transfusion in 0.04 to 0.10%.[4,31] Among medical abortions performed up to 63 days after the last menstrual period, subsequent uterine evacuation occurred in 2.0 to 4.8% of patients and ongoing intrauterine pregnancy in 0.5 to 2.0%.[2,4] In our study among first-trimester abortions, severe adverse events were too infrequent to report an incidence value, 0.04% of the patients underwent blood transfusion, 4.5% underwent uterine evacuation, and 0.13% had an ongoing pregnancy continuing to delivery. Although the incidence of uterine evacuation was increasing before mifepristone had become available, the expected incidence trend after the availability of mifepristone leveled off because of the more rapid increase in the number of abortions (the denominator). Because subsequent uterine evacuation is substantially more frequent after medical abortion than after surgical procedures (<3.0%),[4,37] a practice shift to more medical abortions is expected to increase the incidence of this outcome.

Our study has several potential limitations. The fundamental assumption underlying the validity of interrupted time-series analysis is that outcome trends before the exposure of interest would have continued if the exposure had not occurred. This assumption does not hold if other policy, practice, or contextual changes that may have an effect on outcome incidence occur concurrent to the exposure of interest.[20] However, this analytic approach is robust with respect to changes in the individual-level characteristics of patients or provider practices that accrue gradually over the study period, since such changes are accounted for in trend regression terms during the period before mifepristone had become available. Careful review of policies, academic literature, practice guidelines, and media output that are related to abortion during the study period identified no concurrent changes that would have invalidated our analytic approach. Practitioner fees, training programs, administrative data codes, and cost coverage for the drug were stable during the study period. Surveys and interviews among practitioners indicate that initial mifepristone restrictions were barriers to broad adoption of this practice.[13,38] The short period during which mifepristone was available in Canada with REMS-like restrictions (January 1 to November 6, 2017) precludes a formal analysis of mifepristone availability with restrictions as compared with such availability without restrictions. The unrestricted availability of mifepristone appears to be the fundamental factor associated with changes in our study outcomes.

Our prescription database universally captured mifepristone prescriptions that were dispensed after August 10, 2017 (when a universal no-cost subsidy was introduced) but only captured mifepristone prescriptions from January to August 9, 2017, among patients with income-based prescription subsidies and those under 25 years of age. These factors may have contributed to an underestimation of early mifepristone up-

take. However, this limitation was mitigated by our identification of medical abortions using data regarding practitioner payments, procedures, and prescriptions, along with our exclusion of these months from our time-series analysis. Our population-based data comprehensively captured all abortions among Ontario residents, as well as all subsequent hospital or health service events, even if such services were not provided by the same provider or facility that provided the initial care. Therefore, loss to follow-up was minimal since it involved only patients who had moved out of the province within 6 weeks after the abortion or during the current pregnancy. However, since linkages across databases are possible only for residents who are eligible for provincial health insurance, we excluded the 397 abortions (0.1%) that were provided to nonresidents. Because of lags in availability of cause-of-death data, we could not report the incidence of abortion-related deaths. However, surveillance by the U.S. Centers for Disease Control and Prevention indicates that death is a very rare outcome (2 deaths among 609,095 abortions in 2018).[39] Although minimal data were missing for gestational trimester, we did not have data regarding specific gestational ages in weeks, which prevented an evaluation of changes to abortion timing within trimesters.

When mifepristone became available as a normally prescribed medication in Canada, the frequency of medical abortion rose substantially as compared with the frequency during the period before mifepristone became available, even though the rate of abortion remained materially stable. The incidences of serious adverse events and complications remained materially unchanged, and uterine evacuation and ongoing pregnancy remained infrequent.

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Chemical Abortion Testimony from Toni McFadden, Founder of Relationships Matter

I was 7 weeks pregnant when I went to an abortion clinic about 45 minutes from my home. My boyfriend and best friend accompanied me. I remember feeling like this was the only choice I had to protect myself from the shame of my parents and the embarrassment of my peers.

After getting a sonogram, the nurse told me my baby was only the size of pea therefore it was nothing. In my scared teenage mind, those false words gave my heart comfort to believe I wasn't ending the life of a baby.

I was given the RU486 pill. I was given the first set of pills at the clinic. The doctor said that this would stop the pregnancy. He gave me a bag with another set of pills and instructed me to take them 24 to 48 hours later.

He said I would experience some cramping and bleeding a little heavier than my regular period. I walked out of that clinic and quickly realized I never wanted to go back although they said they would do a follow up with me in about a week.

As instructed, I took the second set of pills 48 hours later at my best friend's house. Her mom was a single mom and wasn't home that weekend. I realized nothing really happened. They had given me two sets of these pills, so I called them the next day. To my surprise they were not as helpful as they were when I initially made the appointment.

When I told the woman on the other end of the phone my experience, she said in an impatient tone, "This is why we gave you two sets of pills. Just take the second set and you will be fine."

I took the second set. I bled a little, but it was not a regular period, and I didn't have any cramping.

In my uneducated mind I thought, well the nurse did say it was only the size of a pea so maybe this was it.

Two months from taking those pills, I would find out I was wrong. I was sitting in class at school and suddenly out of nowhere I started getting these sharp pains. I could barely breathe. I remember someone helping me walk to the nurse's office because I would have never made it on my own.

I ran into the nurse's bathroom and there were blood clots the size of my fist leaving my body. I think I physically and mentally went into shock. I could not believe my eyes or the pain I was experiencing, and, at the same time, I didn't want the truth to come out that I had gotten pregnant.

When the nurse called my mom to tell her what was going on, I lied and said I just had bad cramps.

I remember going home, going straight upstairs to the bathroom, and sat on a toilet for hours bleeding nonstop.

I did not realize or know it then, but I was severely hemorrhaging and probably could have died like the 24 other women that have passed away from taking these very same pills.

The last thing I remember is laying in fetal position in my bed praying and hoping all of this would be over soon.

The physical pain did eventually go away. The mental and emotional scars will always be with me.

[Whereupon, at 12:08 p.m., the hearing was adjourned.]

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