

Rep. Kevin McCarthy (CA-23)

Energy and Commerce Committee

Subcommittee on Health

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THE FUTURE OF MEDICINE: LEGISLATION TO ENCOURAGE INNOVATION AND
IMPROVE OVERSIGHT

Mr. McCarthy, Chairwoman Eshoo, Ranking Member Guthrie, and members of the subcommittee, thank you for including the FORWARD Act (H.R. 5566), which I introduced last fall, in today's hearing.

Fungal Disease Prevalence

Fungal diseases pose a growing public health threat, particularly given limited rapid and accurate diagnostic tests, limited number of available therapies and vaccines, growing resistance to existing drugs, and rising prevalence rates. This includes the disease coccidioidomycosis, more commonly referred to as Valley Fever, which is caused by inhaling spores of the fungus *Coccidioides* largely found in the soil in the American Southwest, although it has now been found as far north as Washington State and can become life-threatening when it disseminates from the lungs throughout the body. According to the CDC's Morbidity and Mortality Weekly Report, Valley Fever incidence in California has increased significantly in recent years, increasing 213% from 2014 to 2018.ⁱ Another fungus - *Candida auris* - has now been identified in over 30 states and are becoming increasingly resistant to available antifungals, prompting the CDC in 2019 to list it as an urgent threat, the highest classification that "requires urgent and aggressive action."ⁱⁱⁱ Further, COVID-19 has led to an increase in fungal infections because of the virus' effect on the immune system and because most treatments for COVID-19, like steroids, can weaken the body's defenses against fungal infections.ⁱⁱⁱ Therefore, to better prepare for

future pandemics and to combat fungal diseases, policies, such as the FORWARD Act, are critical to spur the development of effective and next-generation antifungal drugs and biologics.

Fungal Disease Cost Burden

Fungal diseases range from minor superficial infections to systemic and life-threatening infections. Recent estimates suggest that fungal diseases cost the U.S. healthcare system more than \$7.2 billion in 2017, a conservative estimate given many fungal diseases are underdiagnosed.^{iv} For Valley Fever, some estimate the total lifetime cost burden of cases reported in 2017 in California to be just under \$700 million.^v In Arizona, total lifetime costs of 2019 cases is estimated to be nearly \$736 million.^{vi} Further, these costs are projected to rise with increasing prevalence, as the CDC reports the fungus that causes Valley Fever is now being found in the Pacific Northwest, including south-central Washington State. Kern County, California, which I represent, accounts for more than one-third of all reported Valley Fever cases statewide, or 2,786 of the 8,089 cases reported in the Golden State in 2021.^{vii} Valley Fever and other fungal diseases pose a growing burden on our health care system, in part because of increasing prevalence, but also because diagnostics and treatments are limited.

Lack of Antifungal Drugs and Biologics

There are a limited number of treatments for most fungal diseases and development of antifungal drugs is particularly challenging. For Valley Fever, treatments are few, there is no cure, and there is no vaccine. Importantly, researchers recently successfully tested a Valley Fever vaccine for dogs, with two doses providing high levels of protection.^{viii} There are three main available classes of antifungal drugs, compared to nine classes of antibiotics. The newest class of antifungal drugs, the echinocandins, were discovered in the 1970s and took nearly 30 years to be approved. In fact, only one antifungal drug (isavuconazole), has been approved and marketed in

the last decade for invasive fungal diseases.^{ix} In contrast to antibiotic development, antifungal development is particularly challenging because fungal pathogens are closely related to humans as we are both eukaryotic organisms, making drug toxicity a key concern. Given the very limited number of antifungals in the pipeline, and with fungi becoming even more resistant to multiple classes of existing antifungals, the need for novel antifungal drugs and vaccines is increasingly important and the FORWARD Act would leverage existing government programs to help spur development. With the rising prevalence and cost burden associated with fungal diseases, along with the lack of available antifungal drugs and biologics, Congress has provided funding increases in recent years for the NIH and CDC to bolster scientific research and to enhance awareness of fungal diseases; however, the policy changes included in the FORWARD Act will be critical to build on these efforts in order to reduce the public health threat of fungal diseases.

The FORWARD Act

The Finding Orphan-disease Remedies With Antifungal Research and Development (FORWARD) Act (H.R. 5566) is designed to advance sustained efforts to combat fungal diseases in the short, medium, and long term. In the short term, the FORWARD Act would support basic research for fungal diseases; in the medium term, the bill would streamline FDA approval processes for new antifungal diagnostics, treatments, and vaccines; and in the long-term, the FORWARD Act would incentivize and expedite the development of antifungal vaccines.

Specifically, the FORWARD Act would utilize existing government programs that serve as “push” and “pull” mechanisms to encourage antifungal development. Key provisions of the FORWARD Act include extending QIDP Designation for antifungal biologics, similar to Sec. 501 in the Senate’s PREVENT Pandemics draft bill. Additionally, the FORWARD Act would

codify into law BARDA’s successful CARB-X program and authorize the current spending level of \$500 million to continue to support important preclinical antibiotic and antifungal research. Lastly, the bill would add Valley Fever to the FDA’s PRV program, which serves to provide needed market incentives for the development of drugs for neglected diseases in which there is “no significant market in developed nations” and that “disproportionately impacts poor and marginalized populations.”^x In short, the FORWARD Act provides critical reforms needed to spur antifungal drug and vaccine development.

Conclusion

Fungal diseases like Valley Fever, along with antifungal resistance, pose a significant and growing public health threat. Further, the U.S. is not able to fully reap the benefit of its investment for effective COVID-19 therapeutics as these therapeutics can ultimately make some patients more susceptible to life-threatening and costly fungal infections. Antifungal drug and vaccine development is particularly challenging, and reforms are needed to spur novel antifungals development. The reforms included in the FORWARD Act serve to utilize existing government programs to bolster the antifungal and antibiotic development pipelines, which will be critical to enhance our ability to reduce public health threats from fungal diseases.

Again, thank you for including the FORWARD Act in today’s subcommittee hearing.

ⁱ Hurd-Kundet G, Sondermeyer Cooksey GL, Jain S, Vugia DJ. Valley Fever (Coccidioidomycosis) Awareness — California, 2016–2017. *MMWR Morb Mortal Wkly Rep* 2020;69:1512–1516. DOI: <http://dx.doi.org/10.15585/mmwr.mm6942a2external icon>

ⁱⁱ CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019.

ⁱⁱⁱ Shivakumar Narayanan, Joel V Chua, John W Baddley, Coronavirus Disease 2019–Associated Mucormycosis: Risk Factors and Mechanisms of Disease, *Clinical Infectious Diseases*, 2021; ciab726, <https://doi.org/10.1093/cid/ciab726>

^{iv} Benedict K, Jackson BR, Chiller T, Beer KD. Estimation of Direct Healthcare Costs of Fungal Diseases in the United States. *Clin Infect Dis*. 2019 May 17;68(11):1791-1797. doi: 10.1093/cid/ciy776. PMID: 30204844; PMCID: PMC6409199.

^v Wilson L, Ting J, Lin H, Shah R, MacLean M, Peterson MW, Stockamp N, Libke R, Brown P. The Rise of Valley Fever: Prevalence and Cost Burden of Coccidioidomycosis Infection in California. *Int J Environ Res Public Health*. 2019 Mar 28;16(7):1113. doi: 10.3390/ijerph16071113. PMID: 30925716; PMCID: PMC6480346.

^{vi} Grizzle AJ, Wilson L, Nix DE, Galgiani JN. Clinical and Economic Burden of Valley Fever in Arizona: An Incidence-Based Cost-of-Illness Analysis. *Open Forum Infect Dis*. 2020 Dec 28;8(2):ofaa623. doi: 10.1093/ofid/ofaa623. PMID: 33575419; PMCID: PMC7863867.

^{vii} <https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/CocciinCAProvisionalMonthlyReport.pdf>

^{viii} Lisa F. Shubitz, Edward J. Robb, Daniel A. Powell, Richard A. Bowen, Angela Bosco-Lauth, Airn Hartwig, Stephanie M. Porter, Hien Trinh, Hilary Moale, Helle Bielefeldt-Ohmann, James Hoskinson, Marc J. Orbach, Jeffrey A. Frelinger, John N. Galgiani, Δ cps1 vaccine protects dogs against experimentally induced coccidioidomycosis, *Vaccine*, Volume 39, Issue 47, 2021, Pages 6894-6901, ISSN 0264-410X, <https://doi.org/10.1016/j.vaccine.2021.10.029>.

^{ix} Adriana M Rauseo, Ariella Coler-Reilly, Lindsey Larson, Andrej Spec, Hope on the Horizon: Novel Fungal Treatments in Development, *Open Forum Infectious Diseases*, Volume 7, Issue 2, February 2020, ofaa016, <https://doi.org/10.1093/ofid/ofaa016>

^x (21 U.S.C. 360n)