

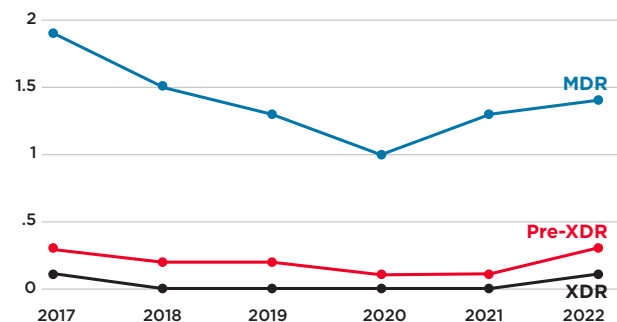
The Path of Least Resistance: Why Drug-Resistant TB Belongs in the BARDA Portfolio

There are many forms of antibiotic-resistant bacteria, but drug-resistant tuberculosis (DR-TB) is one of the most deadly in the world.¹ **In 2022 alone, DR-TB caused an estimated 160,000 deaths globally,² a troubling increase after years of progress. The US has seen a similar trend, with case counts rising in 2021 and 2022 after decades of decline.³** While some of this is likely due to treatment interruptions during the COVID-19 pandemic and resulting lockdowns, TB has long been a moving target for effective antibiotics.⁴ A lack of investment in research and development (R&D) meant that, for many years, the only options for those with certain forms of DR-TB were months of daily injectable medicines that caused debilitating (and sometimes permanent) side effects.⁵ New research in the last decade partially funded by the US government has produced shorter and less toxic options for DR-TB treatment that have transformed the standard of care, but resistance to these newer drugs is already emerging.⁶

Despite the continued need for more innovation in DR-TB treatment, global R&D funding has barely reached half of the estimated financial need.⁷ Some US agencies, such as the National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), and US Agency for International Development (USAID), are already involved in TB research and have contributed to some of the most important recent breakthroughs in TB treatment.⁸ None of these agencies, however, are specifically focused on addressing the threat of drug resistance — nor are they equipped to bring a medical countermeasure to market at the speed necessary to respond

to a newly-emergent outbreak. **Without new TB research partners, the US faces a very near future in which existing regimens for DR-TB lose their potency and people with extensively drug-resistant forms of TB (XDR-TB) have no effective treatment options.⁹**

DR-TB CASE RATES IN THE US, 2017-2022



Source: Centers for Disease Control and Prevention

Fortunately, there is an agency that focuses on antibiotic resistance and has experience successfully responding to airborne pathogens of epidemic and pandemic potential: the Biomedical Advanced Research and Development Agency (BARDA).

In particular, BARDA's focus on antimicrobial resistance (AMR) has been a lifeline to researchers hoping to develop new medical countermeasures. Novel antimicrobials do not have the potential to generate much profit; in order to ensure their appropriate use and stewardship, purchase and uptake will be somewhat limited. Financial and administrative support provided by BARDA helps create a viable pathway for these crucial products by bridging gaps in funding and market access.¹¹ TB researchers face similar challenges

because the US market for TB treatment is largely limited to state and local health departments with limited budgets — which makes DR-TB a perfect candidate for BARDA's involvement.

Another area that BARDA could reshape is that of TB vaccine R&D, which holds significant potential to prevent DR-TB crises. The only currently available TB vaccine, bacillus Calmette-Guérin (BCG), was first administered in 1921 and is still only mostly effective in children under age five and therefore not administered in the US.¹² In response, scientists have been researching a variety of promising candidates in the past few years, including many for use in adolescents and adults, with high efficacy rates.¹³ NIH has provided some crucial funding support, but the need to coordinate research across the fields of immunology, preclinical models, clinical trials,

and manufacturing is still unmet.¹⁴ This role would be filled perfectly by BARDA, which could bring its experience in successfully convening various fields of clinical expertise to bear on delivering lifesaving technologies. In addition, **CDC has classified DR-TB as an antibiotic-resistance “Serious Threat,”¹⁵ making it eligible for BARDA’s portfolio¹⁶ and demonstrating its importance to Americans’ public health.**

BARDA's younger sister agency in Europe, the European Commission's Health Emergency Preparedness and Response Authority (HERA), is already including TB in its scope; BARDA should follow suit. Given DR-TB's eligibility for the research portfolio, variety of potential public and private R&D partners, and public health urgency, BARDA must act now to include DR-TB in its work. The health of millions of Americans depends on it.

ENDNOTES

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