Photo from TB Alliance

# Scaling Life-Saving Interventions Faster
## *Case Studies Series*

### *Pediatric Tuberculosis Treatment*

Tuberculosis (TB) is considered one of the world's most fatal infectious diseases, causing 4,109 deaths per day worldwide. Each year, over 1 million children become ill with TB, which accounts for 11% of the global burden. Traditional methods of diagnosing and treating TB were not suited for children, resulting in over 200,000 deaths per year. This case study presents an overview of key elements that determined the pace of development and uptake of the first child-friendly treatment for TB. These innovative treatments are fixed-dose combination tablets that can quickly disperse in liquid with a palatable fruit flavor.

August 12, 2020

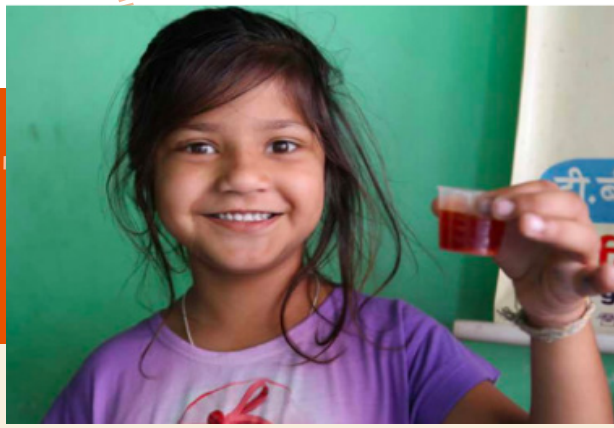
Anshula Nathan, MPH and Elina Urli Hodges, MSPH

*This case study is part of a series that explores pathways and important factors that contribute to the development and uptake of global health interventions—from proof of concept to scale-up.*

LAUNCH & SCALE SPEEDOMETER

Duke GLOBAL HEALTH Innovation Center

LAUNCH & SCALE
SPEEDOMETER



Designed specifically for children with tuberculosis, the fixed-dose combination treatments are fruit-flavored tablets that dissolve in water at the right dosage.

GLOBAL BURDEN OF PEDIATRIC TB: >1 MILLION CHILDREN (2018)[1]

IDEATION TO 1ST COUNTRY LAUNCH: 5 YEARS

NUMBER OF COUNTRIES PROCURING INTERVENTION: 116 (2019)[2]

NUMBER OF TREATMENTS ORDERED: 1,022,922+[2]


**2010**
FIRST DISCOVERY
WHO developes new pediatric TB treatment dosages requirements.[3]

**March, 2011**
IDEATION
Global call to accelerate adoption of new dosages.[4]

**2014**
PROOF OF CONCEPT
WHO issues guidelines with expert panel reviews on child-friendly dosages [5]

**October, 2016**
1ST COUNTRY LAUNCH
Kenya introduced fixed-dose combinations nationwide.[6]

**December, 2017**
WHO PQ
WHO Prequalification application approved.[7]

Every year, more than 1 million children become ill with tuberculosis (TB), which accounts for 11% of the global TB burden.[8,1] In 2017, 233,000 children died from this infectious disease; approximately 96% of these children did not have access to treatment.[9] Many countries have failed to diagnose and treat children accurately, relying on diagnostic methods meant for adults and crushing bitter tasting pills formulated for adults and estimating the appropriate dosage.[13,14,15] These insufficient approaches to diagnosis and care of children with TB have increased this global burden.

While diagnosis remains a challenge, the World Health Organization (WHO) took action in 2010 and revised the treatment guidelines by changing the dosages for children based on new evidence. The WHO also expressed the critical need to engage the pharmaceutical industry in developing new treatments.[3] Despite the expressed urgency, the ill-defined pediatric TB market and poor global demand stifled a response from the pharmaceutical industry.[6,11] In 2011, the WHO and Stop TB Partnership issued a Call to Action during the International Childhood Tuberculosis Meeting to prioritize this global crisis.[4] Although this call sparked the attention of child health advocates and providers in the global TB community, the pharmaceutical industry remained silent. As time passed, the gaps in pediatric TB treatment warranted significant action. In December 2012, Unitaid committed $16.7 million USD to the TB Alliance in an effort to pave the way for child-friendly TB treatments.[10] In August 2013, they launched the Speeding Treatments to End Pediatric Tuberculosis (STEP-TB) initiative to understand the pediatric TB landscape to better define the market for the development of child-friendly treatment.[6,10]

After several years of failed attempts at engaging the pharmaceutical industry, newly developed market data quickly incentivized the sector to act. India-



Photo from TB Alliance, 2017

based Macleods Pharmaceuticals Ltd. entered into a manufacturer cooperation agreement with TB Alliance in March 2014.[11] Within a year, Macleods was the first to accelerate development, leading to two fixed-dose combination (FDC) treatments that quickly dissolve in water and are palatable to children.[6,12]

By December 2015, the treatments were available for purchase through Stop TB's Global Drug Facility (GDF) with an agreed-upon average price of US$15.54 for a full, six-month course. By adhering to the revised dosage requirements, Macleod's applied for WHO Prequalification a month later.[10] Despite the urgent need for this treatment, it took almost two years for WHO to prequalify the FDC treatment.[7] However, STEP-TB's comprehensive in-country adoption efforts facilitated scale up during the waiting period.[6] Much of this success can be attributed to the GDF's close work with The Global Fund to Fight AIDS, Tuberculosis, and Malaria's ad-hoc Expert Review Panel to approve the newly formulated FDCs.[13] The Expert Panel Review approval serves as a trusted endorsement and enables procurement efforts until the WHO prequalification process can be completed. Additionally, WHO and UNICEF issued a joint statement to replace older treatments with the new medicines in March 2017, giving an additional endorsement.[15]

In October 2016, Kenya became the first country to introduce the child-friendly treatment nationwide.[6] Between the first country launch and the end of 2019, more than 90 countries had procured the child-friendly treatment.[2] Comprehensive technical support from GDF enabled a significant leap in the number of countries procuring the treatment—from 36 to 62 countries—in 2017.[6] This support included supply planning, forecasting and quantification, and phasing out old medicines.[13] GDF also developed a tool that allowed countries to adjust their Global Fund grants by estimating the value of wasting existing stock of old medicines and comparing it to the value of purchasing new treatment. This tool expedited procurement and uptake efforts.

With more than 1 million treatment courses ordered to date, STEP-TB's efforts achieved broad impact from introduction to adoption. Additionally, the initiative strengthened the pediatric TB treatment market by accelerating the once-delayed development pathways.

## KEY INSIGHTS

- By having a significant champion in the TB Alliance—along with support from several prominent organizations, such as WHO, USAID, the Global Fund, and Unitaid, and NGOs including Management Sciences for Health (MSH)—children with TB were prioritized across the globe.
- Developing deeper evidence on the once ill-defined pediatric TB market helped mitigate the risk for pharmaceutical companies to develop the treatments.
- In-country preparation—including adoption of WHO dosage guidelines, WHO national TB program guideline implementation, and supply chain strengthening—alleviated adoption barriers.
- GDF's technical support to improve country stock challenges and efforts with the Global Fund to modify grants for procurement expedited countrywide adoption while awaiting WHO approval.

## ABOUT US

The Launch and Scale Speedometer, led by the Duke Global Health Innovation Center, seeks to understand key factors for successful and fast launch and scale of global health interventions to help save lives.

## CONTACT US

**Duke Global Health Innovation Center**
https://dukeghic.org/

**Launch and Scale Speedometer**
info@launchandscalefaster.org
https://launchandscalefaster.org/

## REFERENCES


1. World Health Organization. (2019). Global tuberculosis report 2019. Geneva: World Health Organization; 2019. License: CC BY-NC-SA 3.0 IGO Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf?ua=1

2. TB Alliance. (2019). Accessing Improved TB Medicines for Children. Update from the STEP-TB Project. Retrieved from: https://www.tballiance.org/sites/default/files/assets/TB-Alliance_Child-Friendly-Medicines_pamphlet_2020.pdf

3. World Health Organization. (2010) Rapid Advice: Treatment of Tuberculosis in Children. ISBN 978 92 4 150044 9. Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/44444/9789241500449_eng.pdf;jsessionid=36644AEC6B239207FD896E5EF6A20AC4?sequence=1

4. Stop TB Partnership. (2011). Call to Action for Childhood TB. Retrieved from: http://www.stoptb.org/getinvolved/ctb_cta.asp

5. World Health Organization. (2014). Guidance for national tuberculosis programmes on the management of tuberculosis in children: Second Edition. ISBN 978 92 4 154874 8. Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/112360/9789241548748_eng.pdf?sequence=1

6. TB Alliance. (2017). New Pathways for Childhood TB Treatment: Lessons from the STEP-TB Project. Retrieved from: https://www.tballiance.org/sites/default/files/child-resources/New_Pathways_for_Childhood_TB_Treatment.pdf

7. World Health Organization. (2018). WHO PUBLIC ASSESSMENT REPORT (WHOPAR) Part 1. WHO Prequalification Programme. Retrieved from: https://extranet.who.int/prequal/sites/default/files/TB309part1v1.doc.pdf

8. TB Alliance. (2019). Child-friendly medicines. Retrieved from: https://www.tballiance.org/child-friendly-medicines

9. TB Alliance. (2020). Global Pandemic. Retrieved from: https://www.tballiance.org/why-new-tb-drugs/global-pandemic

10. World Health Organization. (2018). Roadmap towards ending TB in children and adolescents, second edition. Geneva. License: CC BY-NC-SA 3.0 IGO. Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/275422/9789241514798-eng.pdf?ua=1

11. Euro Health Group. (2017). Global Alliance for TB drug development (TB Alliance) Speeding Treatments to End Paediatric Tuberculosis (STEP – TB) End of Project Evaluation. Retrieved from: https://unitaid.org/assets/UNITAID-STEPTB-Final-Evaluation-04July2017.pdf

12. Graham, S. M., Grzemska M., & Gie R. P. (2015). The background and rationale for a new fixed-dose combination for first-line treatment of tuberculosis in children. The International Journal of Tuberculosis and Lung Disease. Retrieved from: https://www.tballiance.org/sites/default/files/child-resources/Background_rationale_new_FDC.pdf

13. Nachman S., Ahmed A., Amanullah F., et al. (2015). Towards earlier inclusion of children in tuberculosis (TB) drugs trials: Consensus statements from an expert panel. Lancet Infect Dis. 2015 June:15(6):711-720. doi: 10.1016/S1473-3099(15)00007-9

14. World Health Organization. (2018). Best practices in child and adolescent tuberculosis. License: CC BY-NC-SA 3.0 IGO. Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/274373/9789241514651-eng.pdf

15. UNICEF. (2018). Change the Game: An agenda for action on childhood tuberculosis. [PDF]

16. World Health Organization, UNICEF. (2017) Statement on the use of child-friendly fixed-dose combinations for the treatment of TB in children. Retrieved from: https://www.who.int/tb/areas-of-work/children/WHO_UNICEFchildhoodTBFDCs_Statement.pdf?ua=1

17. Caminero J. A., Scardigli A. (2016). Tuberculosis in children. Challenges and opportunities. Anales De Pediatria. DOI: 10.1016/j.anpede.2016.10.002