

# Stop TB Partnership's Global Drug Facility

## Update on child-friendly formulations of TB medicines

Virtual Medical Consilium for EURO/TB -Virtual meeting

*24 June 2022*

## Outline

- GDF - Products available for children and adolescents
- GDF Launch Pad – Child-friendly formulations
- GDF - Unique opportunity for countries
- GDF Tools Supporting Procurement and Supply Planning
- Overview of medicines pricing
- Transitioning to new treatment regimens - Key PSM Updates
- Take home points

# WHO consolidated guidelines on the management of tuberculosis in children and adolescents - Products available at GDF (1)

<https://www.stoptb.org/global-drug-facility-gdf/gdf-product-catalog>

## All Products are available at GDF

- **MTB/Rif Ultra cartridges** along with warranties and other auxiliary items for gastric aspirate/stool specimens as the initial Dx test for TB and the detection of R-resistance.
  - *MTB/RIF is being phased out in May 2023 and Xpert MTB/RIF Ultra is recommended by WHO for initial tuberculosis diagnosis and is endorsed to run on 6- AND 10-color modules on all commercially available GeneXpert Systems*
  - *Xpert 6-color systems will be phased out end of June 2022, although continues technical support and replacement parts for the system will be available.*
- The reagents to perform **interferon-gamma release assay (IGRA)** for detection of TBI
- **Child-friendly 3 and 2 FDCs of RHZ, RH, single Ethambutol, adult 4 and 2 FDCs for HRZ(E)/HR** for DS-TB treatment regimens
- All medicines for a **4-month 2HPMZ/2HPM** for DS-TB treatment regimens
- **All adult and child-friendly medicines** including **linezolid 150mg, Delamanid 25mg dispersible tablets and bedaquiline 20mg tablets**, as part of the shorter, all oral longer treatment regimens for DR-TB treatment



**Having the formulations is one step – need to find the kids**

# WHO consolidated guidelines on the management of tuberculosis in children and adolescents - Products available at GDF (2)

All medicines for recommended TPT regimens are available at GDF

## Already in the GDF catalogue

- Rifapentine, 150 mg from Sanofi
- Rifapentine/Isoniazid 300mg/300mg from Macleods Pharmaceuticals

## Two additional formulations are in the pipeline (expected to be included in GDF Catalogue in July 2022)

- 2nd Rifapentine/Isoniazid 300mg/300mg
- Rifapentine 300mg

Both formulations are functionally scored and can be administered to children at the age 2 - 14 years

Table 3.2. Dosing for recommended TB preventive treatment regimens

TPT regimen	Dose by age and weight band <sup>a</sup>					
3HP	Age 2–14 years <sup>c,d</sup>					
	Medicine, formulation	10–<16 kg	16–<24 kg	24–<31 kg	31–<34 kg	≥34 kg
	Isoniazid 100 mg <sup>e</sup>	3	5	6	7	7
	Rifapentine 150 mg	2	3	4	5	5
	Age >14 years					
	Medicine, formulation	30–<36 kg	36–<46 kg	46–<56 kg	56–<70 kg	≥70 kg
	Isoniazid 300 mg	3	3	3	3	3
Rifapentine 150 mg	6	6	6	6	6	
Isoniazid 300 mg + rifapentine 300 mg FDC	3	3	3	3	3	
1HP	Age ≥13 years (regardless of weight band):					
	<ul style="list-style-type: none"> <li>• Isoniazid 300 mg/day</li> <li>• Rifapentine 600 mg/day</li> </ul>					

Source: WHO operational handbook on tuberculosis. Module 5: management of tuberculosis in children and adolescents. Geneva: World Health Organization; 2022

# Pedi DR-TB Formulations available

Cycloserine 125mg  
Ethambutol 100mg  
Ethionamide 125mg  
Levofloxacin 100mg  
Moxifloxacin 100mg  
Pyrazinamide 150mg

Clofazimine 50mg  
Isoniazid 100mg

Bedaquiline 20mg

Delamanid 25mg

Linezolid 150mg

All 11 WHO-Recommended  
DR-TB Medicines  
Now Available & Accessible  
Despite Market Size of  
<1,000 Treatments/Year

**2018**

**2019**

**2020**

**2021**

**2022**



**30-80% Price  
Reductions**

\*Blue indicates 2 suppliers

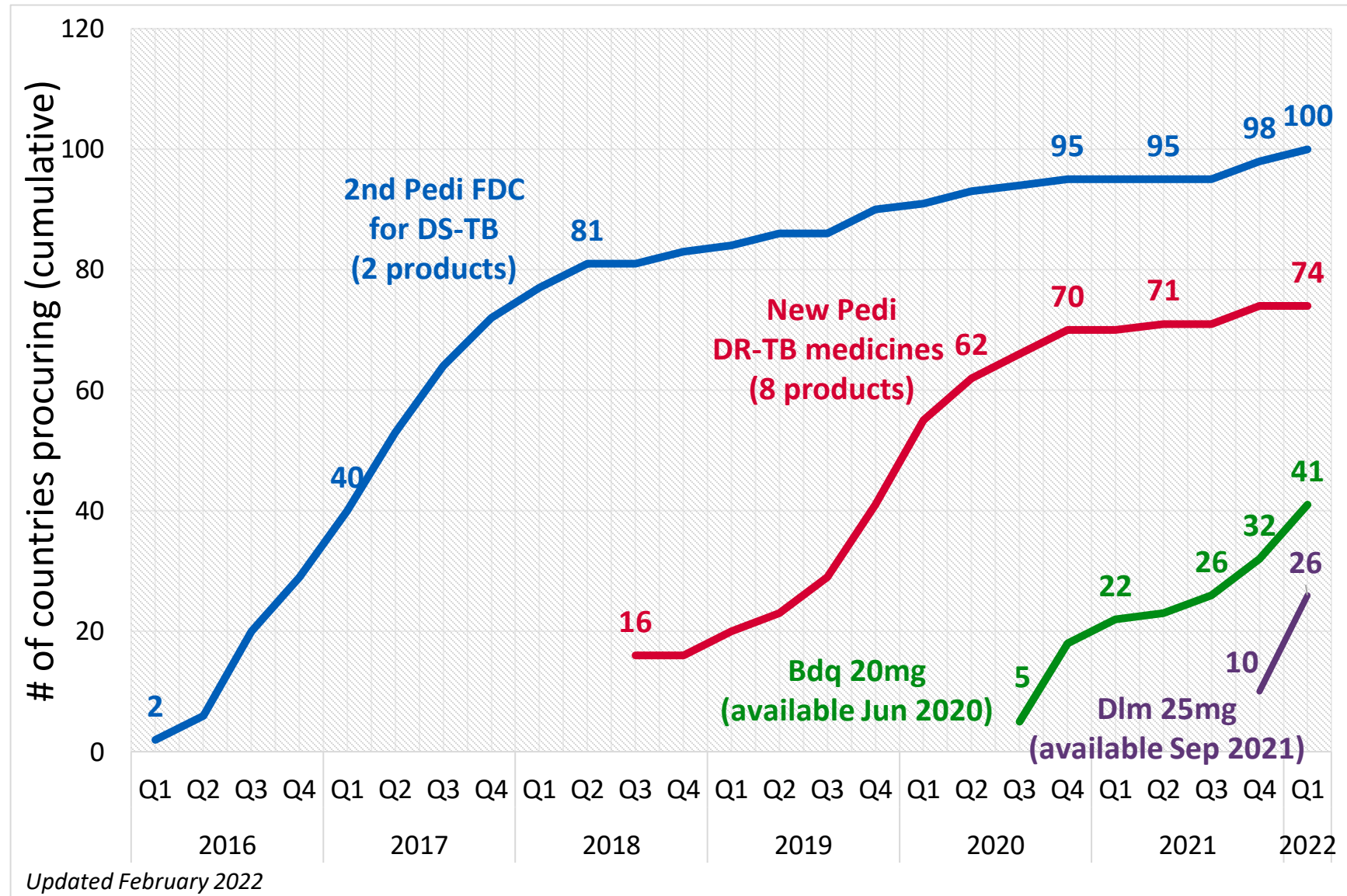
# GDF Launch Pad – Child-friendly formulations

## Peds FDC

- 2 products (generally)
- Standard regimen
- Larger population

## Peds DR-TB

- 11 products
- Individualized regimen
- Smaller population
- Mismatch between order quantities and batch sizes – pooled procurement required



As presented in TPMAT on March 1<sup>st</sup> 2022

Updated February 2022

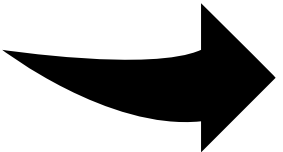
# GDF Launchpad: Child-friendly DR-TB medicines

25,000-30,000 children develop drug-resistant TB each year while only 1,000 children are reported to have been treated

**Objective:** Making new, quality-assured, child-friendly formulations and regimens widely available

**Key Results:**

- Identified **61 adopter countries**
- Created **forecasts** and provide **grants for procurement of medicines to 56 countries**
- Coordinated **country orders w/supplier production plans to meet minimum batch sizes**
- Provided **TA on guideline changes** (via a contract w/Sentinel; in-kind KNCV support)



The initiative provided child-friendly formulations **to treat more than 2500 children in 2020-2022** in participating countries

**Only possible with funding from the Government of Japan & USAID**

# GDF Launchpad: Child-friendly DR-TB medicines in EECA

## Procurement grant provided

Country	Year
Armenia	2019, 2020
Azerbaijan	2019, 2020
Belarus	2018
Georgia	2018
Kazakhstan	2019, 2020, 2021
Kyrgyzstan	2018, 2019, 2020
Moldova	2020
Tajikistan	2018, 2019, 2020
Turkmenistan	2019, 2020
Ukraine	2020
Uzbekistan	2018, 2019, 2020

Since 2018, **11 countries** have received procurement grants for **>600 paediatric DR-TB treatment courses**

Since 2019, About **550 DR-TB kids** have been enrolled on **treatment with pediatric formulations**

*All countries in the region are eligible to procure from GDF*

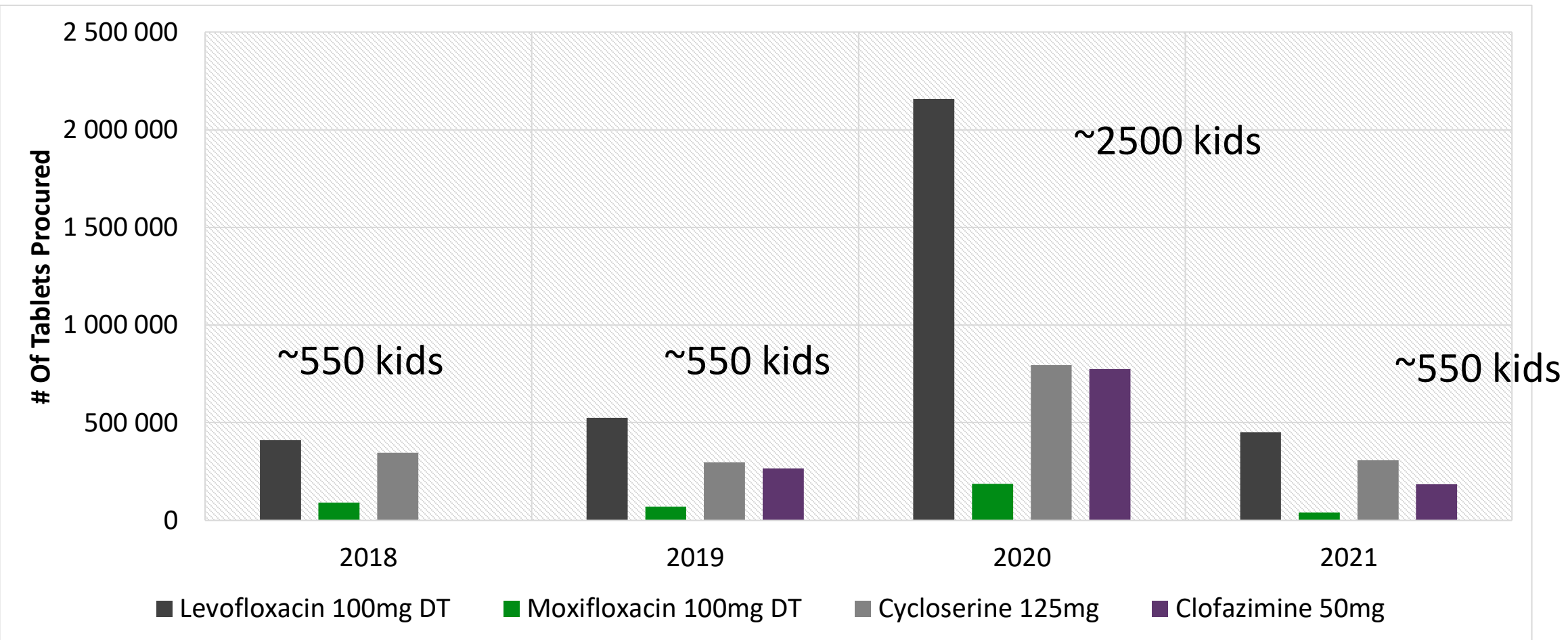
### Challenges:

- *In some countries doctors are not sensitized on the availability and/or use of child-friendly medicines, therefore these medicines are underused*
- *Some countries have not detected at all or detected and enrolled very few DR-TB pediatric cases*
- *To avoid expiries due to underuse, pediatric medicines have been given to adult patients.*

**TA in the clinical management of pediatric DR-TB is available through GDF / Sentinel Project**



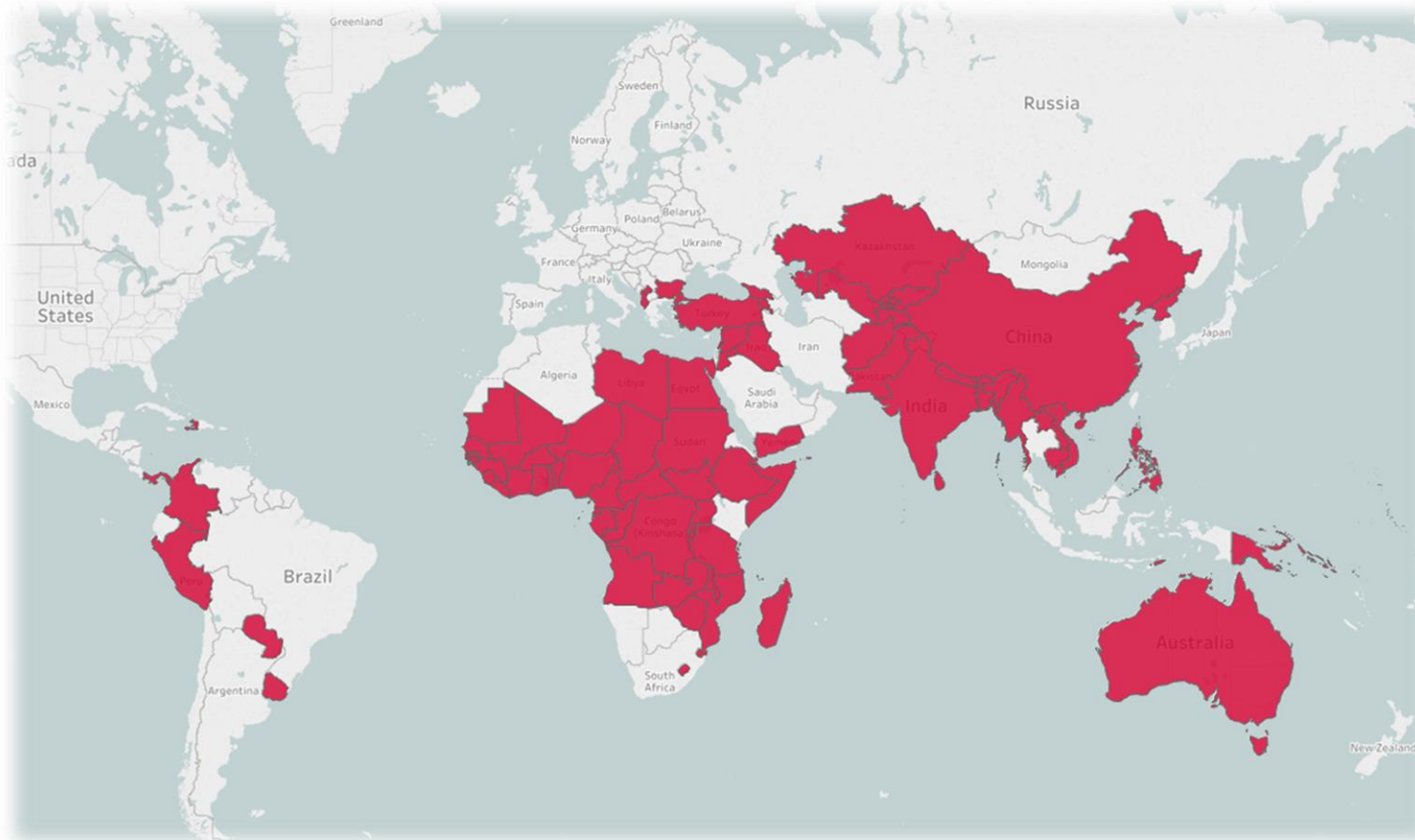
# Overall Volumes of Child-Friendly Formulations Remain Small – need to find the children



As presented in TPMAT on March 1<sup>st</sup> 2022

# Child-friendly FLD formulations

93 countries procured since 2016 including ECA Countries



1. Afghanistan
2. Albania
3. Angola
4. Armenia
5. Australia
6. Bangladesh
7. Benin
8. Bhutan
9. Bulgaria
10. Burkina Faso
11. Burundi
12. Cambodia
13. Cameroon
14. Central African Republic
15. Chad
16. China
17. Colombia
18. Comoros
19. Congo
20. Cote d'Ivoire
21. DPRK
22. DRC
23. Democratic Republic of Timor-Leste
24. Djibouti
25. Egypt
26. Equatorial Guinea
27. Eswatini
28. Ethiopia
29. Gabon
30. Gambia
31. Georgia
32. Ghana
33. Guinea
34. Guinea-Bissau
35. Haiti
36. India
37. Iraq
38. Jordan
39. Kazakhstan
40. Kiribati
41. Kosovo
42. Kyrgyzstan
43. Lao People's Democratic Republic
44. Lebanon
45. Lesotho
46. Liberia
47. Libyan Arab Jamahiriya
48. Madagascar
49. Malawi
50. Maldives
51. Mali
52. Marshall Islands
53. Mauritania
54. Mozambique
55. Myanmar
56. Nauru
57. Nepal
58. Niger
59. Nigeria
60. Pakistan
61. Panama
62. Papua New Guinea
63. Paraguay
64. Peru
65. Philippines
66. Rwanda
67. Samoa
68. Sao Tome and Principe
69. Senegal
70. Sierra Leone
71. Solomon Islands
72. Somalia
73. South Sudan
74. Sri Lanka
75. Sudan
76. Syrian Arab Republic
77. Tajikistan
78. Togo
79. Turkey
80. Tuvalu
81. Uganda
82. United Republic of Tanzania
83. Uruguay
84. Uzbekistan
85. Viet Nam
86. Yemen
87. Zambia
88. Zimbabwe

# GDF - Unique opportunity for countries

**ALL Countries are eligible to procure through GDF, in line with national regulations**

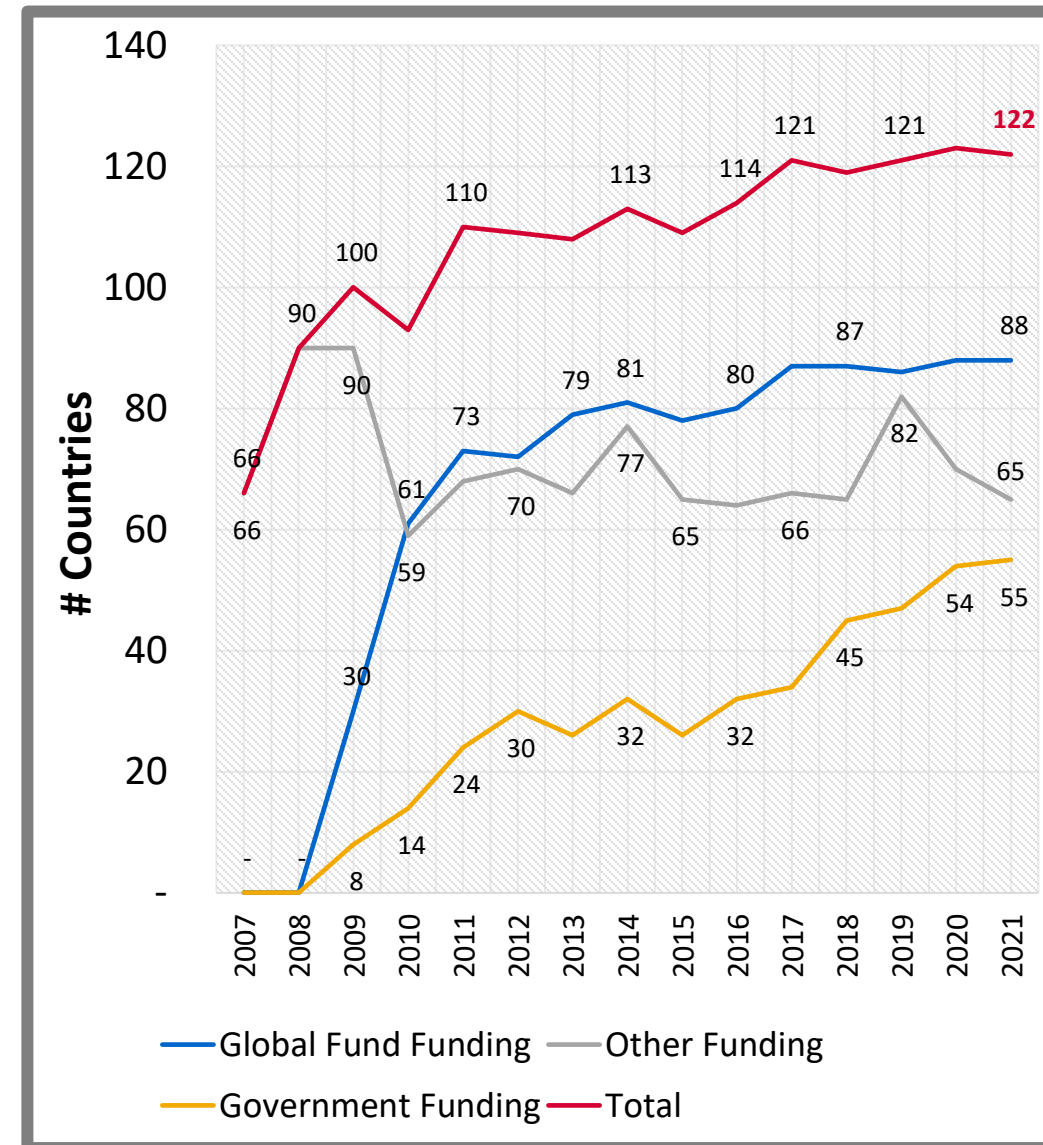
All Funding sources: Government, donor, NGO, Int Org, Research

## GDF Tools supporting procurement

- The online new Procurement Request Form  
<https://www.stoptb.org/place-order/place-order-medicines>
- Strategic Rotating Stockpile
- Flexible Procurement Fund

**Package of comprehensive technical assistance and capacity-building in different aspects of TB PSM to priority countries - managed by**

- 9 Regional Technical Advisers (Two for the EECA region)
- 20+ GDF-trained PSM consultants (USAID supported)



# Tools Supporting Procurement and supply Planning

<https://www.stoptb.org/buyers/plan-order>

- **Category and Product Level Procurement and Delivery Planning Guide**
- **STBP/GDF Budgeting Prices for TB Medicines and Dx**
- **Indicative Reference Costs for Budgeting Purposes**

**Category and Product-level Procurement and Delivery Planning Guide**  
1 June 2022

This document lays out indicative lead-times for planning purposes for TB products procured via the Stop TB Partnership's Global Drug Facility (STBP/GDF).

**Indicative Lead Times**  
1 June 2022

In the context of COVID-19 impacts on supply chain including increased international air and ocean freight capacity constraints, clients are encouraged to place orders earlier than ordinarily to compensate for these constraints.

Procurement and delivery lead-time information is the time from order confirmation and receipt of payment by STBP/GDF to delivery to country. This information is provided at the category and detailed product level and is indicative based on current market knowledge to ensure on-time delivery and best value procurement. Below is a high-level overview of the STBP/GDF ordering process from initial submission of a procurement request form (PRF) until the final order confirmation and payment – when the lead time starts.

**High-Level Overview of STBP/GDF Ordering Process**  
GDF validates quantification and logistics information; works with programmes to get final PRF

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    graph LR
      A[PRF and quantification file submitted to GDF] --> B[GDF provides Price Quote]
      B --> C[GDF receives payment; order is confirmed]
      C --> D[START OF LEAD TIME]
      D --> E[Programme reviews and approves quote and transfers payment]
  
```

Users of this guide should account for country-specific processes related to finalizing the PRF, accepting quotes, and transferring payment when planning procurements.

<https://www.stoptb.org/market-partner-coordination/tb-medicines-dashboard>

## TB Medicines Dashboard

**Adult Drug-Resistant TB Medicines Dashboard**

This dashboard has been developed by Stop TB Partnership/Global Drug Facility in collaboration with USAID, the World Health Organization and The Global Fund to fight AIDS, TB & Malaria. Stop TB Partnership/Global Drug Facility is a US Government contractor under a Contract Commercial Activity Agreement with USAID, a US International Company.

Status:  
 ● Yes  
 ● No  
 ● Ineligible for inclusion  
 ● N/A

Medicines	WHO Guidelines (DR-TB '19)	WHO Guidelines (DR-TB '20)	EMA (submitted)	EMA (2023)	WHO PQ EOI (2023)	WHO PQ (Quarterly Under Review)	WHO PQ listed	Global Fund List of Pharmaceutical Products	Global Fund ERP EOI (New 2020)	Global Fund ERP approved	GDF Catalog
Meropenem 500mg vial	●	●	●	●	●	●	●	●	●	●	●
Meropenem/clavulanate 1000 mg/125 mg vial	●	●	●	●	●	●	●	●	●	●	●
Moxifloxacin 400mg tablet/capsule	●	●	●	●	●	●	●	●	●	●	●
PAS 4gm granules	●	●	●	●	●	●	●	●	●	●	●
PAS Sodium 100gm powder	●	●	●	●	●	●	●	●	●	●	●

DR-TB: Drug-Resistant TB  
 EML: Essential Medicines List  
 EOI: Expression of Interest  
 ERP: Export Review Panel  
 SRA: Strategic Regulatory Authority  
 WHO PQ: World Health Organization Prequalification of Medicines Programme  
 as of: October 2022

Logos: Stop TB Partnership, World Health Organization, The Global Fund

**Sentinel Project Field Guide**  
[http://sentinel-project.org/wp-content/uploads/2022/03/DR-TB-Field-Guide-2021\\_v5.pdf](http://sentinel-project.org/wp-content/uploads/2022/03/DR-TB-Field-Guide-2021_v5.pdf)

<https://www.stoptb.org/gdf-technical-info-note-child-friendly-formulations-dr-tb>

## Technical Information Note, Child-Friendly Formulations for DR-TB

**Management of Multidrug-Resistant Tuberculosis in Children: A FIELD GUIDE**

Fifth Edition, March 2022

**CHILD-FRIENDLY FORMULATIONS FOR DRUG-RESISTANT TUBERCULOSIS**

TECHNICAL INFORMATION NOTE

Ensuring an uninterrupted supply of quality-assured, affordable anti-TB drugs and diagnostics to the world.

stoptb.org/gdf

# Estimated TB Regimen Prices through GDF\* (Valid through June 2022)

Description of Regimen	Regimen Composition	Duration	Weight band	Estimated Regimen Price (USD)
Paediatric DS-TB (Pulmonary)	2RHZE/4RH	6 Months	12-15 kg	\$ 27
	2RHZE/2RH	4 Months	12-15 kg	\$ 19
Paediatric DS-TB (TBM)	2RHZE/10RH	12 Months	12-15 kg	\$ 93
	6RHZEto	6 Months	13-16 kg	\$ 90
Paediatric DR-TB BDQ-based all-oral Shorter Regimen with DT formulations	4 Bdq(6)-Lfx-Cfz-Z-E-Hh-Eto/5 Lfx-Cfz-Z-E	9 Months	10-15 kg	\$653
Paediatric DR-TB all-oral longer regimen with DT formulations	12 Bdq(6) – Lfx – Lzd – Cfz – Cs	12 Months	10-15 kg	\$787

# Transitioning to new treatment regimens - Key PSM Updates

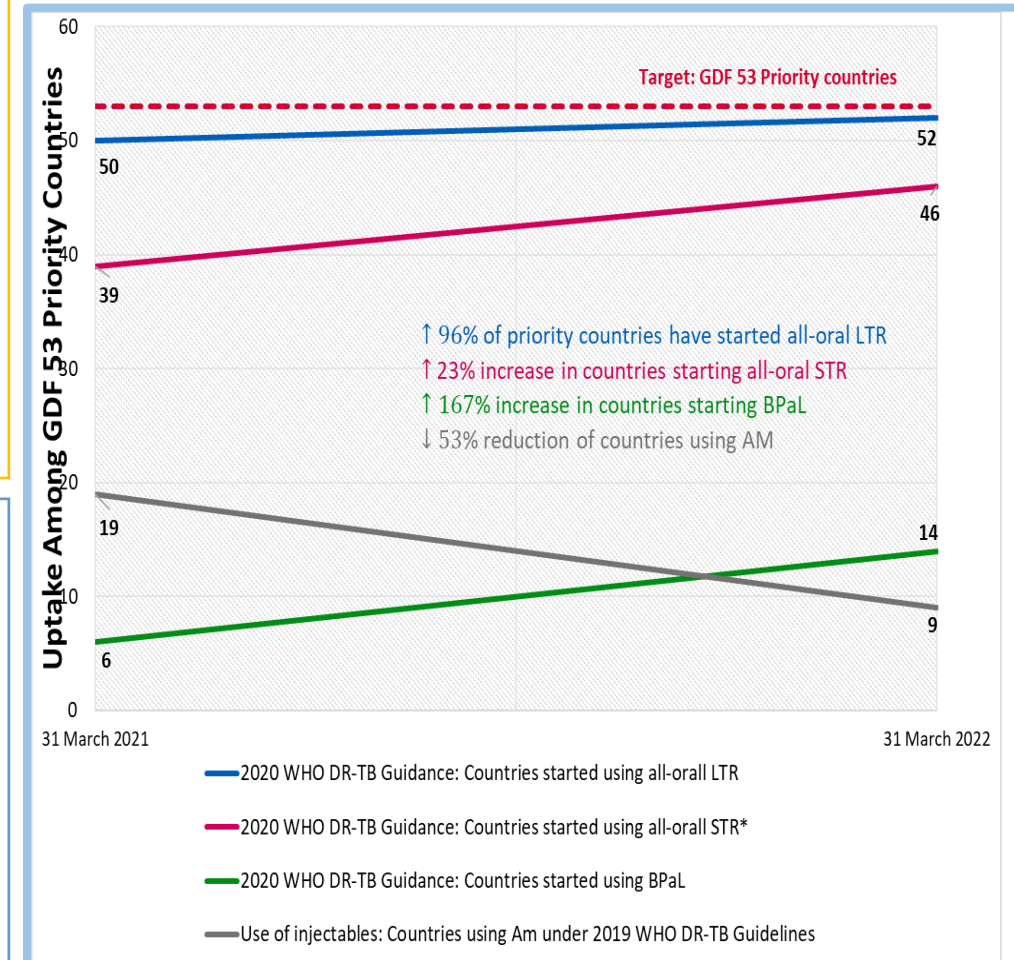
## Challenges

- Complex quantification and forecasting:
  - individualized, DST-based regimens and non-functional TB information systems – *difficult to validate data (specific for EECA countries)*
  - *Slow uptake and rollout of frequently changing recommendations*
- *Decline in notified/enrolled cases (COVID-19 impact) leading to potential overstocks*

## Ways to Address to avoid expiries/stockouts

- **Regular quantification using QuanTB and regularly updated PSM plans including phase-in/phase-out scenarios!**
- **Optimized procurement frequency and availability of buffer stocks**
- **Strong collaboration between GDF and WHO-rGLC: a review of regimens, patient enrollment and transition plans in the PRFs**

## GDF support for the introduction of new WHO DR-TB treatment regimens in 53 PC



# WHO consolidated guidelines on the management of tuberculosis in children and adolescents – Key PSM Updates

## Potential PSM-related Challenges and Solutions for new Guidelines

Table 5.1. Pulmonary TB treatment regimens by age group, disease severity and local epidemiology

Age and severity of TB	Duration and composition of treatment regimen <sup>a</sup>	
	Intensive phase	Continuation phase
<b>Infants aged &lt;3 months or weighing &lt;3 kg</b>		
PTB of any severity	2HRZ or 2HRZE <sup>b</sup>	4HR
<b>Children and adolescents aged 3 months to &lt;12 years</b>		
Non-severe PTB	2HRZ or 2HRZE <sup>b</sup>	2HR <sup>c</sup>
Severe PTB	2HRZE <sup>c</sup>	4HR
<b>Adolescents aged 12–&lt;16 years</b>		
Non-severe PTB	2HRZ or 2HRZE <sup>b</sup>	2HR
Severe PTB	2HRZE <sup>d</sup>	4HR
PTB of any severity	2HPZM	2HPM
<b>Adolescents aged 16–&lt;20 years</b>		
PTB of any severity	2HRZE <sup>e</sup>	4HR
PTB of any severity	2HPZM <sup>f</sup>	2HPM

- Age bands for reporting do not align with recommended age breakdowns for different regimens
- Split between severe and non-severe PTB may not be readily available

Encourage programmes to capture more granular data that can be analysed and aggregated

Source: WHO operational handbook on tuberculosis. Module 5: management of tuberculosis in children and adolescents. Geneva: World Health Organization; 2022

# Take Home Points

- GDF increases access to quality-assured and WHO-recommended products to screen, diagnose, prevent and treat all forms of TB for adults and children:
  - GDF provides TA and capacity strengthening in TB pharmaceuticals' PSM to priority countries (non-priority countries are subject to individual discussion and funding availability) and collaborates closely with the Global Fund, rGLC and other partner/donor organizations
  - GDF's upstream approach to bring in new suppliers, prioritize new product entry and pool demand helps to facilitate new tool entry, encourage competition and create pressure on price for QA medicines as well as reduction of potential interruptions in the supply of TB medicines.
- Updated TB treatment regimes, such as a new 4-month shorter regimen for DS-TB are already reflected in GDF supply planning and supplies and PSM-related technical assistance is available through GDF
- Better uptake and scale-up of paediatric DR-TB medicines are needed in EECA through an early uptake of treatment, and improved case findings, clinical support to doctors and sound PSM systems to ensure access, availability and rational use of TB paediatric formulation.

***TA in the clinical management of pediatric DR-TB is available through GDF / Sentinel Project***



# Thank you!

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