Stop TB Partnership
GLOBAL DRUG FACILITY

XPERT® MTB/RIF AND ULTRA

TECHNICAL INFORMATION NOTE

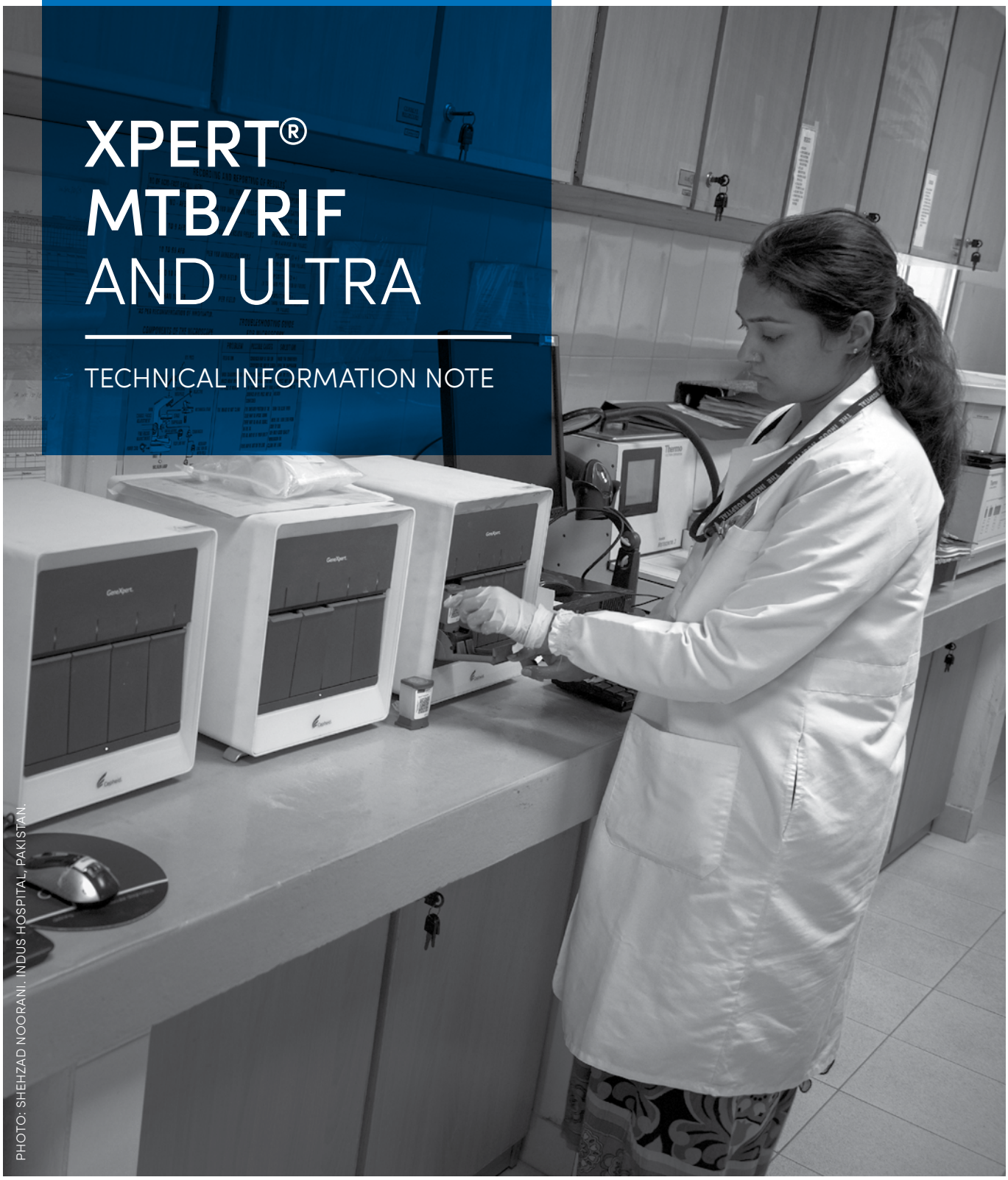

PHOTO: SHEHZAD NOORANI. INDUS HOSPITAL, PAKISTAN.

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

stoptb.org/gdf

Stop TB Partnership
GLOBAL DRUG FACILITY

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TECHNICAL INFORMATION NOTE
XPERT® MTB/RIF AND ULTRA

The Xpert® MTB/RIF test cartridge can simultaneously identify *Mycobacterium tuberculosis* complex bacteria (MTB) and resistance to rifampicin in less than two hours, using the automated GeneXpert® platform. Despite substantial increased sensitivity for MTB detection compared with smear microscopy, Xpert MTB/RIF test sensitivity is nevertheless suboptimal, particularly with smear-negative and HIV-associated TB, and in pediatric populations.
The Xpert® MTB/RIF Ultra test cartridge (Ultra) was developed as a next-generation test, with higher sensitivity for MTB detection especially among smear-negative TB patients as well as more accurate determination of rifampicin resistance. Ultra runs on the same GeneXpert platform as Xpert MTB/RIF, using software version 4.7b or later.

SUPPLY INFORMATION

→ Available in the GDF diagnostics catalog
Manufacturer: Cepheid Inc., Sunnyvale, USA

PRODUCT NAME	Xpert® MTB/RIF kit of 50 test cartridges
GDF ITEM NUMBER	CGXMTB-RIF-50 (Available in the GDF diagnostics catalog)
COST	US $499 for a kit of 50 cartridges (equivalent to US $9.98 per cartridge)*
EXPIRY DATE	Maximum 24 months, minimum 15 months. Due to existing inventory, exact expiry date of a client's lot is only known at time of shipment readiness
STORAGE CONDITIONS	2- 28˚C

* Concessional price offered to the public sector in eligible countries. See page 10 of this Technical Information Note for list of eligible countries.

For more information or to place an order contact
gdf@stoptb.org

PRODUCT NAME	Xpert® MTB/RIF **Ultra** kit of 50 test cartridges
GDF ITEM NUMBER	GXMTB/RIF-ULTRA-50 (Available in the GDF diagnostics catalog)
COST	US $499 for a kit of 50 cartridges (equivalent to US $9.98 per cartridge)*
EXPIRY DATE	Maximum 16 months, minimum 11 months. Due to existing inventory, exact expiry date of a client's lot is only known at time of shipment readiness
STORAGE CONDITIONS	2- 28˚C

* Concessional price offered to the public sector in eligible countries. See page 10 of this Technical Information Note for list of eligible countries.

Test cartridge kits come with individual vials of specimen reagent and individually wrapped sterile, disposable transfer pipettes.

Note: At the time of publication (October 2019), both Xpert MTB/RIF and Ultra are available for ordering, and the manufacturer has indicated that there are no plans to discontinue the manufacturing of Xpert MTB/RIF tests in the foreseeable future.

EQUIPMENT REQUIRED

4-module GeneXpert

16-module GeneXpert

1-module GeneXpert Edge

ITEM	GDF ITEM NUMBER	GDF ITEM DESCRIPTION	COST (IN USD)*
GeneXpert System with 4, 2 or 16 modules	GXIV-4-D, GXIV-4-L	GeneXpert platform, with option of desktop (D) or laptop (L) computer. All GeneXperts come with an initial 2-year warranty on parts.	$17,000, $17,500
	GXIV-2-D, GXIV-2-L**		$11,780, $12,280
	GXXVI-16-D, GXXVI-16-L		$71,000, $71,500
GeneXpert Edge System with 1 module	GXI-EDGE-L	GeneXpert Edge Platform, with tablet and auxiliary batteries. The Edge comes with an initial 2-year warranty on parts.	$8,945
Verification kit (a.k.a. validation pack) for 4-module GeneXpert kit	GX4-4 VAL	Set of dry culture spots to verify initial performance of a new 4-module GeneXpert after installation.	Free of charge
Software upgrade, for use of Ultra cartridges		For laboratories that have existing GeneXpert machines, software 4.7b or later is required to run Ultra. The manufacturer will send a CD to update the software with the initial purchase of Ultra cartridges.	Free of charge

*Concessional prices offered to the public sector in eligible countries. See page 10 of this Technical Information Note.
**The 2-module configuration uses a 4-module shell that allows for later addition of modules if desired (US $3,360 each)

ACCESSORIES REQUIRED

ITEM	GDF ITEM NUMBER	GDF ITEM DESCRIPTION	COST (IN USD)
Sputum containers	106525	80ml each; 1,000 cups per pack	$83.30
Timer	106570	Mechanical timer	$1.11
Latex gloves	106345, 106346, 106347	Sizes small, medium and large, respectively. 1,000 pieces per pack.	$50.32
10% sodium hypochlorite solution	106624	Stable chlorine disinfectant, 100 tablets; 1 tablet should be dissolved in 1 liter of water	$30.25
70% ethanol or isopropyl alcohol solution	106333	70% ethanol/isopropanol, 5 liters	$15.01

Note: Scissors or a pipette tip are required to remove the dried culture spots from a verification kit (a.k.a validation pack) when verifying initial performance of a new GeneXpert

ACCESSORIES OFFERED

ITEM	GDF ITEM NUMBER	GDF ITEM DESCRIPTION	COST (IN USD)
Uninterruptable Power Supply (UPS)	106081	3000 VA / 2100 Watts UPS; alternatively a UPS may be procured locally to allow for direct servicing. Use of a UPS is highly recommended. The internal battery of the offered model allows for continued power during only brief power outages. In settings with extreme incoming voltage fluctuations, a voltage stabilizer may also need to be procured locally.	$1,318.88
Auxiliary battery pack	106491	Battery pack for UPS 3000VA, to amplify the existing back-up time of the UPS up to 150 minutes. In settings with longer power outages, an auxiliary battery pack is required and may be procured locally.	$907.76
For Edge: Power bank external battery, small	850-0535	Battery to provide enough power for running approximately 4 Xpert MTB/RIF tests on Edge.	$99.00
For Edge: Power bank external battery, medium	850-0563	Battery to provide enough power for running approximately 5 Xpert MTB/RIF tests on Edge. Can be connected to the power mains, acting as a UPS. A voltage stabilizer is not required.	$199.00
Solar panel and battery system	106493	Solar panel system for a 4-module GeneXpert, with eight 6V 330AH batteries to allow for 8 hours of operation time.	$9,150.00
Dust filter	700-4510	Dust filter, for use in dusty environments	$350.00
Additional new GeneXpert module	GXIV-Module	Additional new GeneXpert module, for creation of an in-country stockpile (boot stock) or to add capacity to a GXIV-2 GeneXpert	$3,360.00

INSTALLATION AND TRAINING

For new GeneXperts, installations and on-site trainings are free at all sites in major population centers, if the country has a Cepheid office or authorized service provider. Installations outside of major population centers may require additional costs for in-country travel and time of service providers. As an alternative, or when there is no service provider in-country, online trainings are offered at no additional cost.

Additional or refresher trainings may require additional costs for in-country travel and time of service providers.

Users may also be trained at one of Cepheid's training centers in Toulouse (France), Johannesburg (South Africa), São Paulo (Brazil), New Delhi (India). Training is available in English, French, Portuguese, Russian, and Spanish. For details, see: https://cepheidlearn.elmg.net/ets

SERVICE AND MAINTENANCE OFFERED

Warranties only cover parts and shipment, and do not include costs for in-country travel or time of service providers, which needs to be budgeted separately.

For countries interested in pursuing a comprehensive service and maintenance package based on a cartridge surcharge, GDF and partners have developed a model Service Level Agreement that countries can use as a baseline in discussions with their service provider. This document describes basic terms and conditions together with reporting requirements on key performance indicators against targets. For more information, contact gdf@stoptb.org

ITEM	GDF ITEM NUMBER	GDF ITEM DESCRIPTION	COST (IN USD)*
2-year initial warranty		All GeneXperts come with a free 2-year initial warranty. Annual XpertCheck calibration for beginning of year 2 (after year 1) is not included.	Included in cost of system
XpertCheck calibration pack (preventative maintenance)	XPERTCHECKCE- 5	XpertCheck pack for 4 modules, for annual check of calibration. For a site with a GXXVI 16 module instrument, 4 packs are required.	$450.00
XpertCheck calibration pack (preventative maintenance) for Edge	GX-HE-FILTERKIT	XpertCheck pack for Edge, for annual check of calibration. Includes HEPA filter and brush.	$450.00
1-year warranty extension	WX04RG12	1-year warranty extension for a 4-module GeneXpert, including XpertCheck for beginning of year	$2,898.00
	WX02RG12	1-year warranty extension for a 2-module GeneXpert, including XpertCheck for beginning of year	$1,896.00
	WV16RG12	1-year warranty extension for a 16-module GeneXpert, including XpertCheck for beginning of year	$7,800.00
	WX01RG12	1-year warranty extension for a 1-module GeneXpert Edge, including XpertCheck for beginning of year	$1,250.00

3-year warranty extension, bought upfront with a GeneXpert	WX04UP36	3-year warranty extension for a 4-module GeneXpert, including XpertCheck for beginning of years 2, 3, 4 and 5	$6,840.00
	WX02UP36	3-year warranty extension for a 2-module GeneXpert, including XpertCheck for beginning of years 2, 3, 4 and 5	$4,500.00
	WX16UP36	3-year warranty extension for a 16-module GeneXpert, including XpertCheck for beginning of years 2, 3, 4 and 5	$18,504.00
	WX01UP36	3-year warranty extension for a 1-module GeneXpert Edge, including XpertCheck for beginning of years 2, 3, 4 and 5	$3,150.00
3-year warranty extension, bought before end of the first 2 years of initial warranty	WX04RG36	3-year warranty extension for a 4-module GeneXpert, including XpertCheck for beginning of each of the 3 years	$7,902.00
	WX02RG36	3-year warranty extension for a 2-module GeneXpert, including XpertCheck for beginning of each of the 3 years	$5,184.00
	WV16RG36	3-year warranty extension for a 16-module GeneXpert including XpertCheck for beginning of each of the 3 years	$20,898.00
	WX01RG36	3-year warranty extension for a 1-module GeneXpert Edge, including XpertCheck for beginning of each of the 3 years	$3,400.00
Module swap	GX-SWAP-1	A refurbished module(s) is provided to swap out a module(s) requiring calibration or repair. To be purchased when a GeneXpert is not under initial or extended warranty. Shipping costs are additional.	$900.00
Edge instrument swap	EDGE-SWAP	A refurbished instrument is provided to swap out an instrument or module requiring calibration or repair. To be purchased when an Edge is not under initial or extended warranty. Shipping costs are additional.	$900.00

* Concessional prices offered to the public sector in eligible countries. See page 10 of this Technical Information Note.

Examples of country approaches to warranty coverage and XpertCheck calibration:

- **Country A** buys a GeneXpert with 3-year warranty extension at the time of purchase (total of 5 years of coverage). Country does not need to pay for any XpertCheck calibration kits for the 5 year period; Cepheid will send kits for use after years 1, 2, 3 and 4.
- **Country B** buys a GeneXpert and an XpertCheck calibration kit for use after year 1 of the initial warranty. During the second year of initial warranty, country decides to buy a 1-year warranty extension for year 3. Cepheid will send an XpertCheck kit for use after year 2.

- **Country C** buys a GeneXpert and an XpertCheck calibration kit for use after year 1 of the initial warranty. During the second year of initial warranty, country decides to buy a 3-year warranty extension. Cepheid will send XpertCheck kits for use after years 2, 3 and 4.
- **Country D** buys a GeneXpert and an XpertCheck calibration kit for use after year 1 of the initial warranty. During the second year of initial warranty, country decides not to buy a warranty extension. Country continues to buy XpertCheck kits annually to ensure the machine modules are functioning properly, however starting in year 3, country will need to pay for any module swaps and other repairs ad hoc.
- **Country E** buys a GeneXpert and does not buy an XpertCheck calibration kit for use after year 1 of the initial warranty. The second year of the initial warranty is voided. Country will need to pay for any module swaps and other repairs ad hoc starting in year 2. Country should either:
  1. buy an XpertCheck kit as soon as possible to ensure the machine modules are functioning properly, and follow the example of Country D by paying for module swaps and other repairs ad hoc, or
  2. follow the example of Country B or C and buy an extended warranty, which will include an XpertCheck kit.

FORECASTING AND ORDER PLANNING FOR XPERT AND ULTRA

ESTIMATING EXPECTED TESTING VOLUMES

- Forecasting the number of cartridges to be used should use historic consumption forecasting with adjustments, aiming for scale-up to reach targets based on morbidity-based forecasting
- **Consumption-based forecasting:** Forecasting the number of cartridges to be used in a setting using GeneXperts should take into consideration the historic consumption, as well as any foreseen increases in consumption due to expected changes in clinician demand (e.g., changes in diagnostic algorithms or specimen referral), machine functioning (e.g., repaired modules), daily efficiency (e.g., improved staffing, longer working hours), moving of instruments to other sites, or other factors.
  - → If the country experienced stockouts of cartridges or interruption of services for other reasons, past consumption data will underestimate what the consumption would have been if testing had been continuous at all sites. Adjustments will be needed to cover the periods of service interruption.
  - → To facilitate forecasting based on historic consumption, a diagnostic connectivity software may be used to rapidly and accurately assess monthly instrument usage and trends. For more information on diagnostics connectivity solutions, see the GLI Quick Guide to Diagnostics Connectivity Solutions.

- **Morbidity-based forecasting:** Forecasts based on epidemiological data and algorithms may be used as targets for scaling-up use of GeneXpert. All countries should aim to position Xpert MTB/RIF or Ultra as a replacement for smear microscopy to detect TB.
- For guidance on forecasting target numbers of cartridges and GeneXpert modules to procure, see the 2016 WHO Framework of indicators and targets for laboratory strengthening under the End TB Strategy, which includes a spreadsheet for country-specific calculation of diagnostic testing and facility needs using recommended algorithms.

DEVICE THROUGHOUT

- GeneXpert instruments are modular devices, with each module able to operate independently. A module can run up to 4 Xpert MTB/RIF cartridges during a typical 8 hour working day, given the test runtime of 2 hours. As the Ultra cartridge requires a shorter runtime (90 minutes), a module can run up to 5 Ultra cartridges during a working day.
  - → GeneXperts can also run other test cartridges, including for measuring HIV viral load, for early infant diagnosis of HIV, for detection of hepatitis C, sexually transmitted infections and more. Diagnostic integration can provide system efficiencies and cost savings, increase patient access, and improve quality of care. Considerations for adoption and use of GeneXperts in integrated laboratory networks are described in a WHO Information Note.
  - → For a planned new site, the GeneXpert model with the needed number of modules should be selected to test expected volumes. Note a 2-module GeneXpert uses a 4-module shell and allows for expansion of testing capacity.

ORDER SIZES

- The annual number of tests that would be used in 1 year (260 working days) under different scenarios of GeneXpert models and average daily module utilization is provided in Table 1.

Table 1. Number of Xpert MTB/RIF cartridges that would be used in 1 year (260 working days1)

		GENEXPERT MODEL		
		2-MODULE GENEXPERT	4-MODULE GENEXPERT	16-MODULE GENEXPERT
AVERAGE NUMBER OF TESTS PER MODULE PER DAY	4 (100% utilization)	2,080	4,160	16,640
	3 (75% utilization)	1,560	3,120	12,480
	2 (50% utilization)	1,040	2,080	8,320
	1 (25% utilization)	520	1,040	4,160

[1] Number of working days should be adjusted according to country

Table 2. Number of Ultra cartridges that would be used in 1 year (260 working days1)

		GENEXPERT MODEL		
		2-MODULE GENEXPERT	4-MODULE GENEXPERT	16-MODULE GENEXPERT
AVERAGE NUMBER OF TESTS PER MODULE PER DAY	5 (100% utilization)	2,600	5,200	20,800
	4 (80% utilization)	2,080	4,160	16,640
	3 (60% utilization)	1,560	3,120	12,480
	2 (40% utilization)	1,040	2,080	8,320
	1 (20% utilization)	520	1,040	4,160

[1] Number of working days should be adjusted according to country

SUPPLY PLANNING: SUGGESTED DELIVERY FREQUENCY

- The supply plan must account for the procurement and supplier lead times as well as t he time required for country-specific importation processes; in total this may entail 4-6 months. The time required for in-country distribution must also be considered.
- For planning of orders and shipments, the size of an order may include all of the cartridge needs estimated for a year, though with more than 1 shipment.
- Note the expiry date of Ultra cartridges may be as low as 11 months at time of shipment readiness. The maximum expiry date is expected to increase over time, similar to the standard Xpert MTB/RIF cartridges.
  - → Shipments of Ultra cartridges may therefore be required at least twice a year in order to avoid the risk of stock-outs.
  - → For Xpert MTB/RIF cartridges, given the relatively long expiry date (at least 15 months), shipments may be made annually.
  - → For sites running Ultra for the first time, the GeneXpert software may require an update (version 4.7b or later) using a compact disc provided with an initial shipment of Ultra cartridges. Any possible delay in updating the software should be factored into the initial shipment size.

COST PER XPERT TEST

- GeneXpert testing requires neither batching nor external controls, so the running costs for testing a patient sample is limited to the test cartridge (which comes with the required specimen reagent and transfer pipette), a sputum container and gloves.
- Costs for service and maintenance of instruments, including warranties (or annual XpertCheck kits and module swaps, if warranties are not bought) and in-country travel and labor of service providers, as well as trainings, should also be considered when budgeting.

LIST OF COUNTRIES ELIGIBLE FOR CONCESSIONAL PRICING

Country list and original pricing for cartridges, equipment and service and maintenance negotiated by FIND. Updated pricing for cartridges (US$ 9.98) negotiated by USAID, PEPFAR, Gates Foundation and UNITAID for August 2012-2022.

LOW INCOME	LOWER MIDDLE INCOME	UPPER MIDDLE INCOME	HIGH INCOME
Afghanistan	Angola	Albania	Antigua & Barbuda
Benin	Bangladesh	Algeria	Argentina
Burkina Faso	Bhutan	American Samoa	Barbados
Burundi	Bolivia	Armenia	Chile
Central African Republic	Cabo Verde	Azerbaijan	Croatia
Chad	Cambodia	Belarus	Estonia
Comoros	Cameroon	Belize	Guam
Congo, Dem. Rep.	Congo, Rep.	Bosnia and Herzegovina	Latvia
Eritrea	Côte d'Ivoire	Botswana	Lithuanaia
Ethiopia	Djibouti	Brazil	Palau
Gambia, The	Egypt, Arab Rep.	Bulgaria	Panama
Guinea	El Salvador	China	Seychelles
Guinea-Bissau	Georgia	Colombia	St. Kitts and Nevis
Haiti	Ghana	Costa Rica	Trinidad and Tobago
Korea, Dem. People's Rep.	Honduras	Cuba	Uruguay
Liberia	India	Dominica	All other high income countries
Madagascar	Indonesia	Dominican Republic	
Malawi	Kenya	Ecuador	
Mali	Kiribati	Equatorial Guinea	
Mozambique	Kosovo	Fiji	
Nepal	Kyrgyzstan	Gabon	

Eligible for concessional prices

Have received concessional prices exceptionally

Not eligible for concessional prices

LOW INCOME	LOWER MIDDLE INCOME	UPPER MIDDLE INCOME
Niger	Lao PDR	Grenada
Rwanda	Lesotho	Guatemala
Senegal	Mauritania	Guyana
Sierra Leone	Micronesia, Fed. Sts.	Iran, Islamic Rep.
Somalia	Moldova	Iraq
South Sudan	Mongolia	Jamaica
Syrian Arab Republic	Morocco	Jordan
Tajikistan	Myanmar	Kazakhstan
Tanzania	Nicaragua	Lebanon
Togo	Nigeria	Libya
Uganda	Pakistan	Macedonia, FYR
Yemen, Rep.	Papua New Guinea	Malaysia
Zimbabwe	Philippines	Maldives
	São Tomé and Principe	Marshall Islands
	Solomon Islands	Mauritius
	Sri Lanka	Mexico
	Sudan	Montenegro
	Swaziland	Namibia
	Timor-Leste	Nauru
	Tunisia	Paraguay
	Ukraine	Peru
	Uzbekistan	Romania
	Vanuatu	Russian Federation
	Vietnam	Samoa
	West Bank and Gaza	Serbia
	Zambia	South Africa
		St. Lucia
		St. Vincent and the Grenadines
		Suriname
		Thailand
		Tonga
		Turkey
		Turkmenistan
		Tuvalu
		Venezuela, RB

Not classified by World Bank
Cook Islands
Niue
Tokelau
Western Sahara

Eligible for concessional prices

Have received concessional prices exceptionally

Not eligible for concessional prices

WHO TECHNICAL EXPERT GROUP RECOMMENDATIONS ON ULTRA (JANUARY 2017)

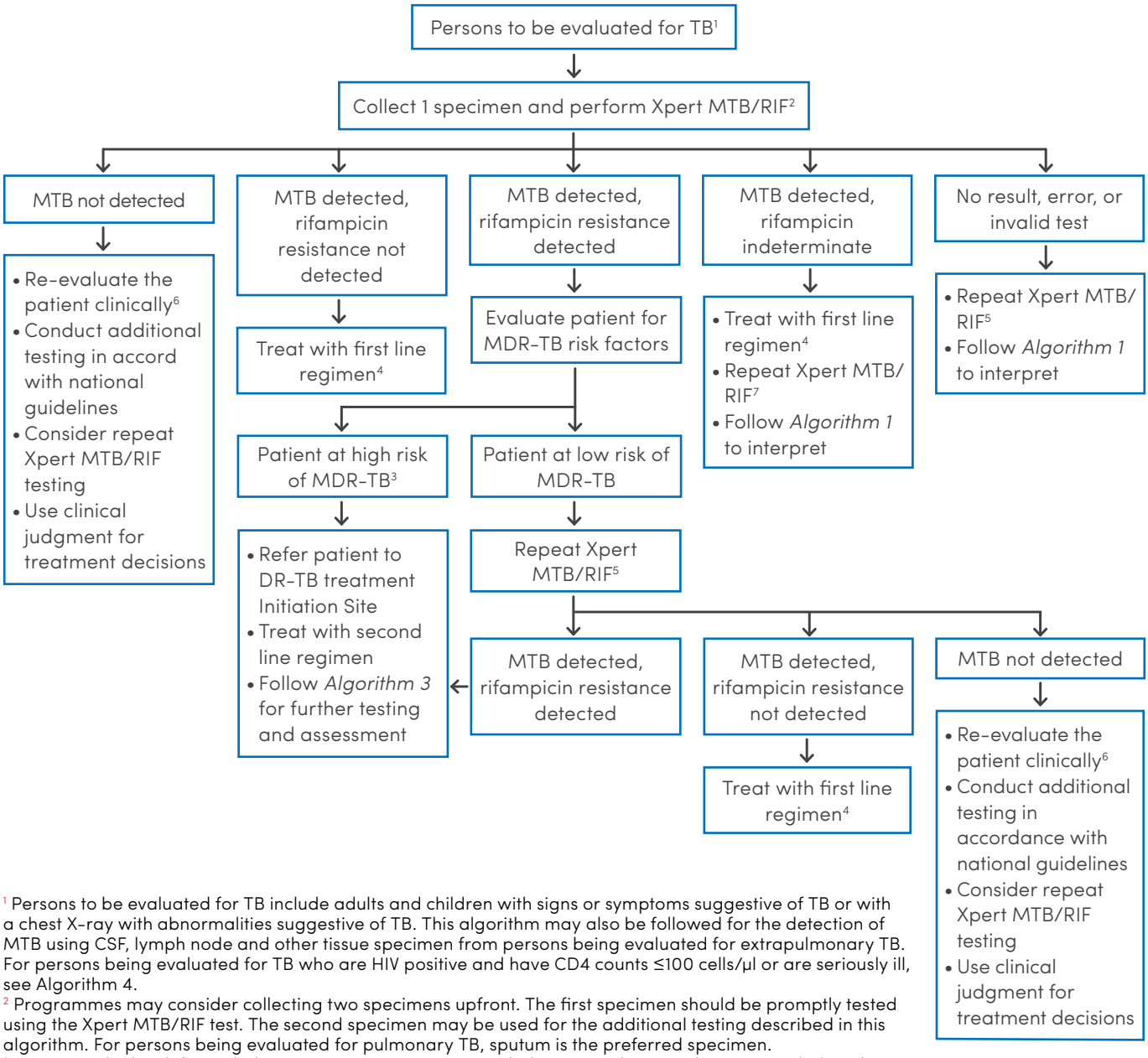
In January 2017, a Technical Expert Group met to analyze a multi-centre non-inferiority diagnostic accuracy study conducted by FIND of Xpert MTB/RIF Ultra compared with Xpert MTB/RIF for the detection of MTB and rifampicin resistance. Upon assessment of the study findings, they made the following statements regarding use of Ultra:

- Ultra is non-inferior to the Xpert MTB/RIF assay for the detection of MTB and rifampicin resistance and can be used as an alternative to the latter in all settings.
- The current WHO recommendations for the use of Xpert MTB/RIF (see reference 2 in the Resources available below) also apply to the use of Ultra as the initial diagnostic test for all adults and children with signs and symptoms of TB and in the testing of selected extrapulmonary specimens (cerebrospinal fluid, lymph nodes and tissue specimens).
- The interpretation of Ultra results for MTB detection are the same as for Xpert MTB/RIF with the exception of "trace calls".
  Interpret "trace calls" as follows: Among persons with HIV, children and extrapulmonary specimens "trace calls" should be considered to be true positive results for use in clinical decisions and patient follow-up; Among persons not at risk for HIV, with an initial "trace call" positive result, a fresh specimen from the patient should undergo repeat testing and the result of the second Ultra test be used for clinical decisions and patient follow-up.
- Ultra can be used on all GeneXpert instrument platforms and is suitable for use at central or national reference laboratory level, regional and district levels. GeneXpert has the potential to be used at the peripheral level, provided uninterrupted electricity supply and temperature conditions can be ensured.

RESOURCES AVAILABLE: CURRENT NORMATIVE AND PRACTICAL GUIDANCE

1. 2017 WHO Meeting Report of a Technical Expert Consultation: Non-inferiority analysis of Xpert MTB/RIF Ultra compared to Xpert MTB/RIF. Report describes performance of Ultra and the basis for WHO recommendations on Xpert MTB/RIF to apply to Ultra
2. 2013 WHO Policy Update: Xpert MTB/RIF Assay for the Diagnosis of Pulmonary and Extrapulmonary TB in Adults and Children. WHO recommendations calling for Xpert MTB/RIF as the initial diagnostic test for people with signs or symptoms of TB, as well as for detecting pediatric or extrapulmonary TB
3. 2017 GLI Guide on Planning For Country Transition to Xpert MTB/RIF Ultra Cartridges. Topics include: Adapting national guidelines and diagnostic algorithms; Managing existing cartridge supply, forecasting, procurement and distribution; Planning site-level computer software upgrades and trainings of laboratory personnel and clinicians; Ensuring coordination among donors and partners supporting Xpert implementation in countries; Monitoring impact of the roll-out of Ultra.
4. 2018 GLI training package on implementation of Xpert MTB/RIF and Ultra. Modules include: TB biosafety; Specimen collection & referral; Procurement and inventory management; Recording & reporting results; Monitoring quality indicators; Quality assurance of Xpert MTB/RIF and Ultra; External quality assurance; Clinical guide to Xpert MTB/RIF and Ultra.
5. FIND implementation resources, including checklists on pre-installation and installation; clinical site monitoring and evaluation; comprehensive site visit assessment, supervision (troubleshooting)
6. 2016 FIND/CDC/PEPFAR Providing Uninterrupted Power for GeneXpert in Low and Middle Income Settings: A Practical Guide: guidance on GeneXpert power backup solutions to meet different power supply scenarios

POSITIONING OF THE XPERT MTB/RIF TEST IN ALGORITHM 1 OF THE **GLI MODEL TB DIAGNOSTIC ALGORITHMS**



[1] Persons to be evaluated for TB include adults and children with signs or symptoms suggestive of TB or with a chest X-ray with abnormalities suggestive of TB. This algorithm may also be followed for the detection of MTB using CSF, lymph node and other tissue specimen from persons being evaluated for extrapulmonary TB. For persons being evaluated for TB who are HIV positive and have CD4 counts ≤100 cells/µl or are seriously ill, see Algorithm 4.

[2] Programmes may consider collecting two specimens upfront. The first specimen should be promptly tested using the Xpert MTB/RIF test. The second specimen may be used for the additional testing described in this algorithm. For persons being evaluated for pulmonary TB, sputum is the preferred specimen.

[3] Patients at high risk for multidrug-resistant TB (MDR-TB) include previously treated patients including those who had been lost to follow-up, relapsed, and failed a treatment regimen; non-converters (smear positive at end of intensive phase); MDR-TB contacts; and any other MDR-TB risk groups identified in the country.

[4] Patients should be initiated on a first-line regimen according to national guidelines. A sample may be sent for molecular or phenotypic DST for isoniazid if the patient has been previously treated with isoniazid or if there is a high prevalence of isoniazid resistance not associated with rifampicin resistance (i.e., isoniazid mono- or poly-resistance) in this setting or for DST for rifampicin if rifampicin resistance is still suspected.

[5] Repeat Xpert MTB/RIF test at the same testing site with a fresh specimen. Interpret the result of the repeat test as shown in this algorithm. Use the result of the second Xpert MTB/RIF test for clinical decisions.

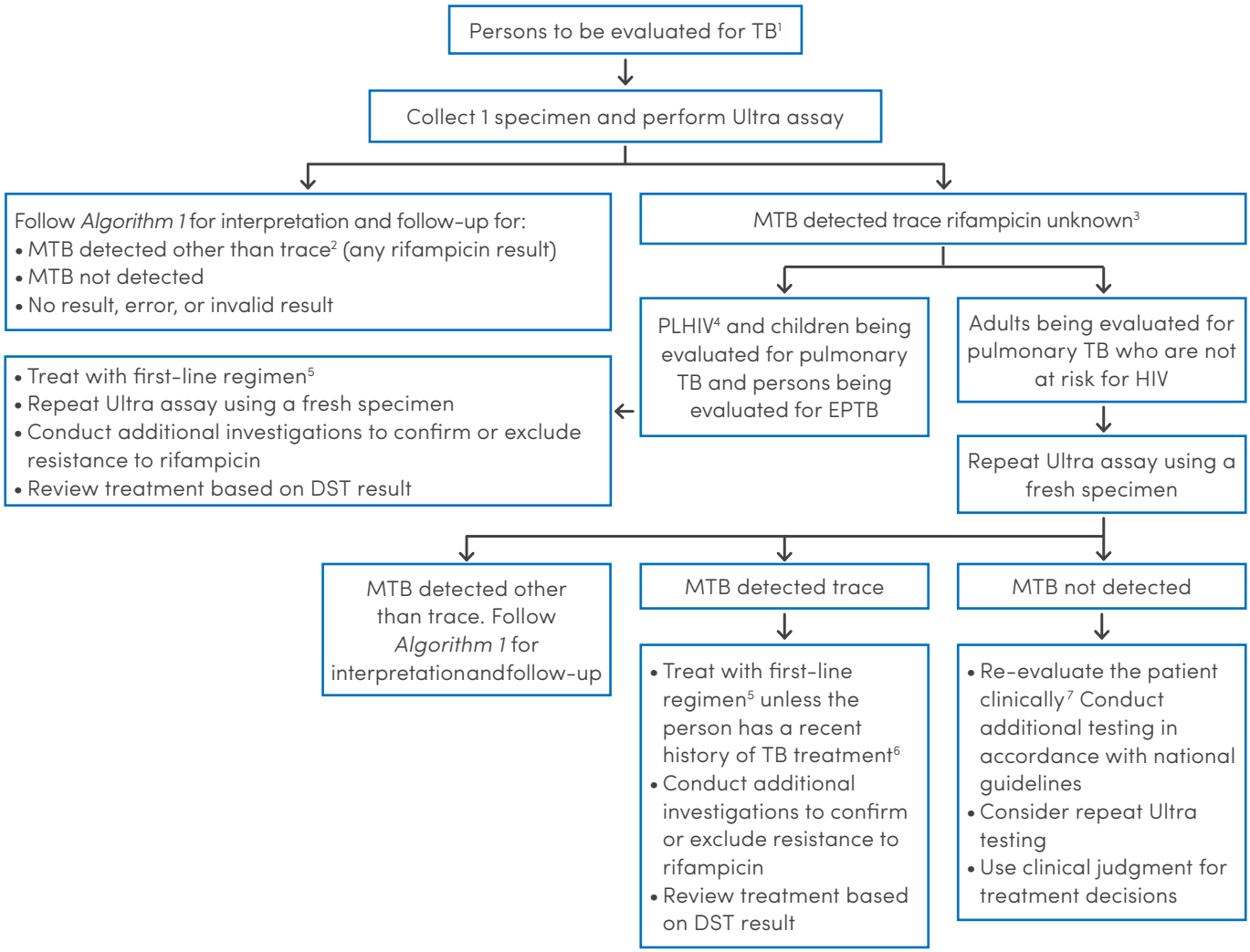
[6] Further investigations for TB may include chest X-ray, additional clinical assessments, clinical response following treatment with broad-spectrum antimicrobial agents, repeat Xpert MTB/RIF testing, or culture. For diagnosis in children, also use a score chart for diagnosis of TB in children according to national guidelines.

[7] Repeat Xpert MTB/RIF test at the same testing site with a fresh specimen. Use the rifampicin result of the second Xpert MTB/RIF test in this algorithm for a decision(s) regarding choice of regimen (first line or second line regimen).

POSITIONING OF XPERT MTB/RIF ULTRA IN ALGORITHM 1a OF THE **GLI MODEL TB DIAGNOSTIC ALGORITHMS**

As published in the 2017 GLI Guide on Planning for Country Transition to Xpert MTB/RIF Ultra Cartridges

Algorithm 1a. Algorithm for universal patient access to rapid testing to detect MTB and rifampicin resistance incorporating Xpert MTB/RIF Ultra



[1] Persons to be evaluated for TB include adults and children with signs or symptoms suggestive of TB or with a chest X-ray with abnormalities suggestive of TB. This algorithm may also be followed for the diagnosis of extrapulmonary TB using CSF, lymph node and other tissue specimen. The evaluation should include determining the person's age, HIV-infection status, and possibility of a history of TB treatment.

[2] MTB detected (not trace) includes MTB detected high, moderate, low, or very low. Follow Algorithm 1 for interpretation and follow-up testing.

[3] MTB detected trace results do not provide any information regarding rifampicin susceptibility or resistance.

[4] PLHIV include persons who are HIV positive or whose HIV status is unknown, but who present with strong clinical evidence of HIV infection in settings where there is a high prevalence of HIV or among members of a risk group for HIV. For all people with unknown HIV status, HIV testing should be performed according to national guidelines.

[5] Patients should be initiated on a first-line regimen according to national guidelines unless the patient is at very high risk of having MDR-TB or if a second Ultra assay indicates rifampicin resistance. Such patients should be initiated on an MDR-TB regimen.

[6] For adults who successfully completed a course of therapy within the past 2 years (i.e., recent TB treatment), the possibility of both Ultra trace results being false-positive results because of the presence of non-viable bacilli must be considered. Clinical decisions must be made on all available information and clinical judgment; further investigations for TB may include chest X-ray, additional clinical assessments, clinical response following treatment with broad-spectrum antimicrobial agents, repeat Ultra testing, or culture.

[7] Further investigations for TB may include chest X-ray, additional clinical assessments, clinical response following treatment with broad-spectrum antimicrobial agents, repeat Ultra testing, or culture.

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