The Cepheid buy-down agreement: Evaluation and implications for the future

Summary from November 2019 Report

Background

Following the endorsement of Xpert MTB/RIF (Cepheid, CA, USA) as a diagnostic test for tuberculosis (TB) and rifampicin-resistant TB (RR-TB) by the World Health Organization (WHO) in December 2010, the test was initially introduced at a reduced price of 16.86 USD per cartridge, and 17,000/17,500 USD per 4-module instrument (desktop/laptop), which represented at that time, a reduction of 75 percent and 60 percent, compared to normal market prices, respectively. The reduced prices were made available to the public sector of 145 countries and territories. A stepwise cartridge price reduction scheme was foreseen whereby the cartridge price would gradually decrease dependent on annual cartridge volume sales, starting at 16.86 USD per cartridge for more than 600,000 cartridges and reaching 9.98 USD per cartridge once sales exceed 4.7 million cartridges per year.

In 2012, an immediate reduction of prices was achieved by the U.S. Agency for International Development (USAID), the U.S. Department of State's Office of the Global AIDS Coordinator (OGAC) , Unitaid/WHO, the Bill & Melinda Gates Foundation (the "buy-down agreement"); which guaranteed a price of 9.98 USD per cartridge immediately and for the following 10 years, instead of waiting for the price to be repeatedly reduced following cartridge procurement volumes. In order to guarantee these even further reduced prices, USAID, OGAC, Unitaid/WHO and the Bill and Melinda Gates Foundation provided a total of 11.1 million USD to the manufacturer Cepheid. Reduced prices were made available for the same, previously determined 145 countries – more specifically for the public sector, including governments and government-funded institutions, non-governmental organizations (NGOs), United Nations organizations, and donors and funding mechanisms supporting eligible countries.

Since the introduction of Xpert MTB/RIF, several important policy and product changes occurred. Initially recommended by WHO to be used for TB and RR-TB detection of risk groups, WHO updated their policy recommendation to use Xpert MTB/RIF for all patients with signs and symptoms of TB (hereafter called the "Xpert4All policy"). In 2017, Cepheid introduced a new Xpert MTB/RIF cartridge version with superior sensitivity to the market (Xpert MTB/RIF Ultra). This is also available at the same concessional price of 9.98 USD per cartridge. Cepheid has also begun the development of cartridges to test for other drug resistance aside from rifampicin.

The buy-down agreement ends in 2022, and this evaluation was conducted to determine impact and implications for the future. This evaluation focuses on coverage of the buy-down agreement, past cartridge and module procurement, and projections of future needs. Access of the private

sector as well as service, maintenance, and repair systems and needs have been assessed. Lastly, a review of Xpert impact on clinical outcome measures has been conducted. This evaluation analyzed implications for the future and provides recommendations to inform the development of a future strategy.

Discussion and Recommendations

As a result of this evaluation, five key topics have been identified, which are of high relevance for decision making regarding a possible extension of the buy-down agreement and/or for negotiations about conditions for a buy-down extension:

- Access and accessibility of concessional prices for currently eligible customers;
- Service, maintenance, and repair systems;
- Private sector access to concessional prices;
- Global systems for monitoring and support; and
- Future needs, feasibility, affordability, and future strategy for Xpert use and expansion.

Access and accessibility of concessional prices for eligible customers

The buy-down agreement ensured a reduced price for the Xpert technology in more than 130 countries. Those countries account for more than 99 percent of the global TB and RR-TB disease burden, presenting the excellent coverage of the buy-down agreement.

Since the introduction of Xpert into the market, 45.9 million Xpert MTB/RIF cartridges were delivered under concessional prices, 96 percent of which (44.0 million) from 2013 onwards, i.e. the year after the buy-down agreement was signed.

While the current coverage of the buy-down agreement is excellent, a number of observations suggest that not all eligible countries access, or are able to easily access, the contractually agreed reduced prices for Xpert cartridges or modules though.

Cartridge and instrument/module delivery data provided by Cepheid indicate that 14 eligible countries have never received any items at concessional prices (neither cartridges nor modules). Among those are countries, evidence suggests, that Xpert testing is indeed used in the public sector (for example, scientific publications report this from Latvia, Lithuania, and Croatia). It has been speculated that those countries procure through a local distributor, which does not pass on the reduced prices to the eligible customers. It was not possible to further evaluate the situation within the scope of this analysis, but there is an urgent need for further investigation; complete sales data from Cepheid for individual countries, stratified by the health sector and prices charged, would greatly improve the understanding of the current situation.

It is well known that national procurement regulations in countries, which often allow payment only upon delivery of orders, do conflict with Cepheid's requirements for pre-payment in USD. Consequently, countries, which use domestic funding, procure through local distributors that

might allow payment upon delivery and/or in local currency. Those local distributors, mostly commercial companies, certainly charge for their services and the potential risk for payment default and currency fluctuations, which adds to the overall costs for Xpert in countries. There is anecdotal evidence justifying very high charges applied by local distributors, but the charges need to be reasonable and importantly, local distributors should be obliged to pass on the reduced item prices to customers, if these are eligible for a reduced price.

An alternative way to access concessional prices is procurement through the Global Drug Facility (GDF), which guarantees the reduced prices and charges an additional three percent for services, thus representing a very suitable alternative for countries, especially those which are charged high prices by the local distributor. Of note, the risk of payment default for GDF is currently mitigated through a USAID-supported flexible procurement grant, which would be required to continue if GDF will continue its services.

There is also some information that neither Russia nor China can currently access concessional prices for cartridges, which would explain the unexpected pattern of item delivery observed. It was not possible to validate and completely understand the current situation or history of events in those two countries, but this requires further investigation.

If access to concessional prices is difficult, limited, or even denied to certain countries, it would certainly limit the coverage and impact of the buy-down agreement, especially considering the high disease burden in Russia and China alone. Consequently, formalizing and regulating access and accessibility to concessional prices, including the role and charges of local distributors, is required. The end of the buy-down agreement and potential future negotiations with Cepheid offer a great opportunity to address these topics.

Therefore, it is recommended to:

- Conduct further in-depth analysis of sales to eligible countries and prices charged by the health sector, to confirm that all eligible customers can and do access concessional prices, or if that is not the case, to understand the reasons.
- Local distributors should be obliged to pass on the reduced price to eligible customers in the respective countries, and extra charges should be quoted separately. This could be regulated in a future Memorandum of Understanding (MoU) with Cepheid.
- Cepheid should be requested to more closely monitor and regulate charges and conditions applied by local distributors, for example, by determining a maximum ceiling for service charges that can be demanded by local service providers. While it is not known which type of agreements Cepheid currently makes with local distributors, a franchise-like system could be considered, which will allow Cepheid to standardize conditions and charges at national levels. A ceiling value for local distributor charges could also be addressed in a future MoU with Cepheid.
- A future buy-down agreement should also clarify under which conditions a country can be formally denied access to concessional prices, and whether or not that can be a decision made solely by Cepheid, or if it must agree with the collaborators in the MoU.

Ideally, a decision to exclude a country from the eligibility list should be a decision by all signatories to the MoU.

Service, maintenance, and repair systems

Service, maintenance and repair systems, as well as their effectiveness, remain global challenges. While the number of countries with a local partner has been increasing over the past years, and Cepheid made efforts to establish regional repair centers, the overall coverage is still insufficient given that 58 of 150 eligible countries still do not have a local partner (among those are several high-volume procurement countries such as Tajikistan, Sudan, and the Democratic Republic of Congo).

Insufficient coverage and quality of service, maintenance, and repair has been observed in several other factors during this evaluation. It has been noted that the majority of local partners do not keep a buffer stock of modules, which would be actually considered a minimum standard of quality. The relatively high module failure rate reported among the ten surveyed countries emphasizes the importance of having access to timely repair or module replacement to avoid service interruptions.

The time-to-repair was found to be on average very reasonable (approximately two weeks) for modules/instruments covered by any type of warranty or service level agreement (SLA) in the surveyed countries; there are however exceptions. In Pakistan, for example, the local service provider self-reported a repair time of 40 days. These data are not stratified by the warranty coverage status, but Cepheid reported themselves that 100 percent of instruments are covered by a warranty/SLA in Pakistan. Therefore, this repair duration is unacceptably long.

When asked about main reasons for long repair times (more than two weeks), four of nine countries indicated the response to service/repair requests by Cepheid as the main problem. An additional four countries stated that the response by Cepheid is one driver of delay among others, but not the main.

It is very much a concern that about one third of countries have less than 25 percent of their instruments covered by any warranty/SLA, which likely contributes to additional costs, time to repair, and service interruption. Given the high costs of warranty extensions, the lack of funding in countries can be assumed to be one of the main reasons for the poor service and maintenance coverage.

While only a few countries have been offered the AccessCare model to date, and it yet has to be seen how this develops in the future. There are a number of concerns that should be addressed (for example the lack of standardization and transparency of pricing). Currently, several organizations and donors are supporting countries in individual surcharge negotiations with Cepheid, either through facilitation of information exchange, contract template development, or reviewing and advising on individually offered contracts and conditions. For those countries, i.e.

countries with support from a large donor or NGO, this support in negotiations will limit the risk of countries agreeing to inadequate or overly expensive conditions. However, countries without this type of support are at risk to pay very high prices or agree to unfavorable conditions, especially because Cepheid has not published a transparent pricing scheme for the AccessCare model.

Despite efforts made to develop one single global surcharge price (or several regional surcharge prices) that will be applied to all countries, there was no overall agreement on the value and/or conditions associated. Subsequently, Cepheid has continued with individual country negotiations. Volume-based cartridge surcharge prices will be very beneficial for high-volume countries, such as South Africa, eventually, and low-volume countries will be disadvantaged given their lower negotiation power. Since in a global or regional pricing model, high-volume countries would effectively pay a higher price than the price they would be able to negotiate individually, there is little buy-in from several high-volume countries on this model. It is indeed not very likely that a standardized global surcharge price can be negotiated, and individual negotiations will continue.

Consequently, there is an urgent need for transparency, standardization, and especially, a long-term plan for a service, repair, and maintenance scheme in the future. The end of the buy-down agreement and potential future negotiations with Cepheid offer an opportunity to formalize the system.

It is recommended to consider the following aspects in future negotiations with Cepheid:

- Cepheid needs to publish a transparent pricing scheme for surcharge prices, depending on volume of cartridges. These should be part of the standardized AccessCare contract and its conditions, which are currently developed with partner support. The published standardized pricing scheme will help countries avoid agreeing to unfavorable prices or conditions, especially smaller countries without technical support from donors or NGOs.
- There should be a maximum surcharge value negotiated with Cepheid.
- Cepheid could offer both systems in parallel, i.e. AccessCare and extended warranty contracts. Countries should be allowed to choose the model themselves, depending on their needs. In order to be practicable, it should be one system only for a country and not a mix of both, which will also facilitate a transparent AccessCare pricing scheme.
- Current discussions and negotiations focus also very much on current warranty coverage of instruments, which is justified, but a long-term solution is required. The final AccessCare pricing scheme should, under the assumption that it will be a one country/one system approach, publish prices independent of current warranty coverage. That will allow countries to plan and budget accordingly and make decisions now about procurement of extended warranties.

Private-sector engagement

There was little evidence found during this evaluation for a substantial market expansion into the private-for-profit (PFP) sector. Several countries engaged with individual private facilities and supply them with cartridges and/or equipment under certain conditions, but those efforts have been of limited scope. These findings from a selected set of countries are in line with recent publications on access and prices of Xpert in the private sector.

The importance of expanding eligibility criteria for concessional prices had been already recognized early by the collaborators for the buy-down agreement in 2012. However, no evidence has been found that Cepheid has initiated major attempts to make cartridges or instruments available at concessional prices to the private sector. In order to be more conclusive, a more comprehensive, larger scope investigation across more countries needs to be conducted. In addition, actual sales data from Cepheid by the health sector would greatly support this investigation.

While direct and immediate access to concessional prices for the private sector would be certainly beneficial, it will be important to consider monitoring and evaluation systems to ensure prices charged to the patients do not include cartridge costs, to ensure quality of care in private facilities, and to guarantee detected cases are notified to the National TB Program (NTP). These cautions have been noted before.

Two initiatives have been identified in which private sector consortia negotiated access to concessional prices with Cepheid (India and Philippines). These could serve as examples for other countries. Eventually, this type of model can grant access to reduced prices for private sector facilities. This would subsequently reduce patient costs, but also allow for a monitoring system to ensure quality of care is provided and detected TB cases are notified to the NTP.

In the context of future buy-down negotiations, the following recommendations should be considered:

- Adopting the approach from the two consortia examples from India and the Philippines, the eligibility criteria for access to concessional prices for PFP sites could be formally published, which would allow any future initiatives or consortia to access concessional prices without having to negotiate with Cepheid individually.
- The conditions should include (adopted from the Initiative for Promoting Affordable and Quality TB Tests, IPAQT) a maximum price that can be charged for an Xpert test; the adherence of the private sector to NTP guidelines for diagnosis, treatment, and care of patients; the obligation to notify detected cases to the NTP, and an established monitoring and supervision system through the NTP.

Global systems for monitoring and support

While many high-burden countries are well supported by donors and organizations, there is currently no global oversight mechanism that monitors procurements or conditions and quality

of local distributors and service providers in all countries. As outlined before, this could have led to a situation in which countries face challenges with access and accessibility of concessional prices and problems with their local distributors and service providers. In the future, countries will be at risk for agreeing to high surcharge costs or unfavorable AccessCare contract conditions.

GDF has been partly fulfilling a role for country support on many of the aforementioned topics, and has been able to solve many conflicts between countries and Cepheid in the past. Currently, however, GDF does not have the mandate or the means to provide a global monitoring and support system to all countries.

- Based on findings of this evaluation, a global monitoring and support mechanism that serves all countries should be established to ensure access and accessibility of concessional prices, ensure fair prices for future AccessCare negotiations, and to support monitoring and trouble-shooting for conflicts with local partner services and costs.
- It is important that this type of mechanism would also provide support to small countries and/or countries without large NGO or donor support.
- This mechanism could be formalized in an MoU with Cepheid and ideally include a more comprehensive and detailed data sharing obligation by Cepheid.
- It could be considered to give the mandate of global monitoring and support mechanisms to GDF, given GDF partly executes that role already. This might, however, require additional support for human resources and other means, including but not limited to the flexible procurement fund to mitigate the risk for customer payment default.

Future needs, feasibility, affordability, and strategy for Xpert use and expansion

In 2017 and 2018, Xpert cartridge sales were constant around 11.5 million cartridges per year in 136 eligible countries. Xpert uptake and rollout exceeded expectations, as the current annual sales represent more than 2.5 times the volumes anticipated when the initial reduced-price negotiations were held with Cepheid. The volume of cartridges delivered to eligible countries did not substantially increase anymore in 2018 compared to the previous year, but individual trends in countries with the highest procurement volumes show an increasing trend. This reflects the continuing expansion of Xpert testing in high-burden countries, which is expected to continue in the coming years.

The maximum market potential for Xpert MTB/RIF cartridge sales globally was projected at 104.4 million cartridges per year in 168 of 216 countries. This volume would be needed if all countries use Xpert for all presumptive TB patients, target 90 percent performance, and conduct contact tracing.

The vast majority of the 97 percent (101.3 million cartridges) would be needed in currently eligible countries. At the current price of 9.98 USD per cartridge, this requires 1,011.4 million USD per year in eligible countries. The corresponding global number of capacity of modules needed at medium utilization would be 206,941, which represents a value of 924.9 million USD. In eligible countries, the capacity of 144,712 modules would be needed (615 million USD). At

least for eligible countries, an approximate investment of 201.3 million USD in modules has been already made.

The Xpert4All at 90 percent, even without contact tracing, is likely unrealistic to be achieved in the coming years, as a major scale up of TB and HIV program activities and a substantial increase in funding in eligible countries are required. The current investment for Xpert cartridges, (11.5 million cartridges per year) are not even sufficient for all countries to provide Xpert testing for risk groups, which would require 23.5 million cartridges per year at the 90 percent target.

In a more moderate scenario, countries would implement their respective policies stepwise at (at least) a 60 percent and 75 percent performance target. To reach a 60 percent detection target, 28 countries need to scale up their performance; to achieve a 75 percent performance target, 59 need to scale up their program activities. For eligible countries only, these goals require 53 million and 57.7 million cartridges per year (for 60 percent and 75 percent actual policy). Applying respective prices, these cartridges have a value of 529 million and 576.1 million USD. The corresponding number of modules are 75,773 and 82,434, which have a value of 322 and 350.3 million USD respectively. At least for eligible countries, an approximate investment for 47,357 modules (201.3 million USD) has already been made.

In addition, costs for unsuccessful tests (plus approximately eight percent) and costs for service and maintenance have to be added. The expected costs for service and maintenance are currently difficult to estimate, given the ongoing introduction of the AccessCare model, for which Cepheid has not published transparent pricing schemes. If every country would implement their actual policies at least at 60 percent or 75 percent, the annual service, repair and maintenance costs would be 47.9 and 52 million USD if the AccessCare model would be implemented; or 54.9 and 59.7 million USD per year, if all countries would continue to purchase annual warranty extensions. These estimates are, however, based on very simple assumptions, and especially for the AccessCare model, will likely change.

In summary, considering cartridge costs, unsuccessful tests, and service and maintenance, implementing current policies at 60 percent requires approximately 620 million USD per year; implementing at the 75 percent target requires approximately 675 million USD per year. There will be substantial additional costs for module procurement, at approximately an additional 121 and 149 million USD, and actual in-country implementation (for example, for training and lab infrastructure).

Conclusions and recommendations:

- At the current costs for cartridges and equipment, implementing Xpert4All in all (currently eligible) countries will not be affordable, and the prices need to substantially drop. This should be negotiated with Cepheid
- New price negotiations should use projected cartridge and module requirements for the moderate target scenarios, i.e. all countries implement their current policies at (at least) 60 percent and 75 percent targeted case detection.

- Additional costs for unsuccessful tests and maintenance schemes substantially add to projected costs and need to be considerably reduced as well. As mentioned before, Cepheid should publish a transparent pricing system, independent of current instrument warranty status, which subsequently can be used to project annual costs and benefits.

To request the full report, please contact Amy Piatek at apiatek@usaid.gov.